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पुस्तकालय

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पुस्तक पर किसी प्रकार का निशान लगाना वर्जित है। कृपया १५ दिन से अधिक समय तक पुस्तक अपने पास न रखें।

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इस तिथि सहित १५वें दिन तक यह पुस्तक पुस्तकालय में वापिस आ जानी चाहिए। अन्यथा ५ पैसे प्रतिदिन के हिसाब से विलम्ब-दण्ड लगेगा ।

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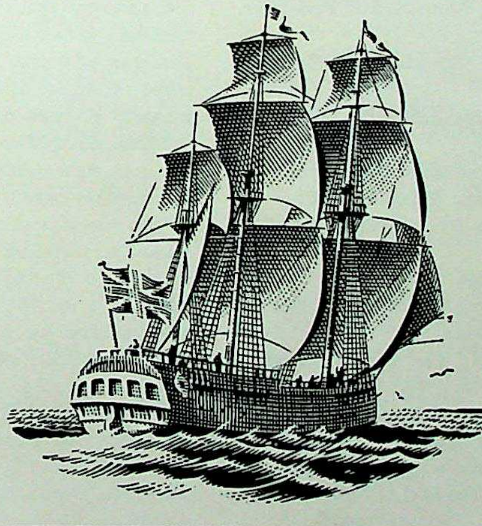

ENDEAVOUR

A review of the progress of science, published in five languages

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The European Space Research Organisation

Current negotiations to extend political and economic co-operation between western European countries have attracted worldwide interest; it is much less well known that co-operation in the scientific field has been widely established for some ten years and is now to be considerably extended. As far back as 1952, the plans were laid that led to the establishment of a laboratory for research in high-energy nuclear physics at Geneva. This laboratory, known as CERN (*Organisation Européenne pour la Recherche Nucléaire*), is now in full operation, and involves the active co-operation of scientists and technologists from twelve countries—the United Kingdom, France, Germany, Italy, Sweden, Norway, Denmark, Austria, Belgium, the Netherlands, Spain, and Switzerland. Space research also needs exceedingly expensive equipment. It is therefore not surprising that similar arrangements should be discussed in this field also. In June 1962, the official representatives of nine of these countries signed an agreement to establish the European Space Research Organisation (ESRO); Austria, Denmark, and Norway have yet to sign. The agreement now awaits ratification.

The aim of ESRO is to conduct purely scientific research. It will not concern itself primarily with the development of large booster rockets or of the associated launching facilities, but will purchase these. It is, however, specifically proposed that ESRO should operate a range for launching smaller rockets of the type used for vertical atmospheric sounding.

The proposed research programme has three subdivisions. The first involves the use of sounding rockets for a wide variety of atmospheric studies up to altitudes of about 200 km—altitudes too low for satellites to be used. Particular interest attaches to the study of the atmosphere at high latitudes, as many of the properties involved are influenced by the Earth's magnetic field. In agreement with the Swedish Government it is proposed that a range for launching these rockets should be established just north of Kiruna, where there is already a geophysical observatory, as well as excellent urban facilities not readily available elsewhere in Arctic latitudes. In addition, ESRO will arrange for sounding rockets to be launched from nationally operated ranges in Europe; the proposed rate of launching, when everything is in full operation, is about fifty rockets a year.

The second programme depends on the use of satellite vehicles carrying moderate payloads, of about 75 kg, launched into near-Earth orbits—out to say 1500 km—without any special facilities for orientation. The Anglo-American satellite Ariel is of this type. Such satellites can provide a great deal of important information about the outer part of the Earth's atmosphere, particularly the ionosphere. The rockets to be used for launching these satellites, and the facilities for launching them, will be purchased.

Thirdly, there are two major programmes that require powerful rocket boosters. One of these involves launching satellites weighing about 1000 kg into near-Earth orbits. These will be equipped with instrument platforms that can be maintained, to an accuracy of seconds of arc, in a desired orientation with respect to the fixed stars. Astronomical instruments may be mounted on such platforms to carry out observations of heavenly bodies at ultraviolet and X-ray wavelengths; such wavelengths are completely inaccessible at the ground, or even at balloon altitudes, because of atmospheric absorption. A considerable portion of ESRO resources will be devoted to this programme.

It is also planned to establish space observatories, with a scientific payload capacity of about 100 kg, in orbit round the Moon. In this way it will be possible to observe radiation systematically, at distances of about 400 000 km from the Earth, while carrying out observations important for lunar physics. Again, large booster rockets will be required.

For the major programmes, the booster rockets and launching facilities will be purchased, and an independent European Launcher Development Organisation (ELDO), which could provide both rockets and facilities, is in an advanced planning stage. The launcher uses the British Blue Streak as first stage, with second and third stages developed by France and Germany respectively. Italy, Holland, and Belgium will be responsible for various auxiliary facilities, and the launching site will be the Woomera rocket range in Australia.

It is hoped that the sounding-rocket programme will be in operation within a year of ratification of the agreement; that the first astronomical satellite will be launched within six years; and that the first lunar observatory will be in operation within eight years. The first of the smaller satellites will be launched within three years. No plans exist for any programme involving a man in space.

It is proposed that, in general, the scientific experiments to be carried out in the sounding-rocket and small-satellite programmes will be the responsibility of scientific groups in universities and other research establishments. ESRO will be responsible for the satellite engineering and for ensuring that apparatus within a particular payload is compatible. The cost of the scientific instruments will be borne by the national group concerned, but all other costs will be borne by ESRO. As close co-operation between different groups with apparatus in the same payload is essential, this involves no departure from the principle of European co-operation in this scheme. The scheme has the great advantage of associating with ESRO a wide variety of research groups in the different countries.

The scale of the major programme, however, is so great that it is proposed that ESRO shall carry full responsibility for the satellite engineering and also for the scientific payload, although ESRO may arrange contracts with research groups from national universities and other institutions. In these programmes ESRO will bear the entire costs.

To implement these various programmes, ESRO will include a headquarters in Paris and a Space Technology Institute (ESTEC) at Delft; a Data Analysis and Vehicle Tracking Centre (ESDAC) at Darmstadt; and a laboratory (ESLAR) in Italy. All institutes will be staffed on an international basis. Of these institutes, ESTEC will be by far the largest. It will provide all the engineering facilities for the satellite and rocket payloads, and will be responsible for the major programmes. In addition, it will carry out research in all the relevant branches of advanced technology.

ESDAC will analyse data from space vehicles and, in addition, will supervise any satellite-tracking and telemetry-receiving stations that may be established by ESRO. To avoid duplication, there will be the closest possible co-operation with other countries on this matter. The laboratory in Italy will be concerned with basic research studies associated with the programmes.

It is proposed that the annual budget will build up to a sum of about £16 000 000 in six years' time, including the cost of launching vehicles and facilities. The contributions from the different countries are based on the same considerations as were agreed for CERN; the United Kingdom will contribute 25 per cent of the total.

As planned, ESRO should make a very substantial contribution to space science without incurring expenditure out of proportion to that involved in other expensive branches of pure science. The proposed ESRO annual budget for six years hence is only a little over twice that of CERN at the present time.

Buoyancy mechanisms of sea creatures

E. J. Denton

Many sea creatures can control their density and so save themselves a great deal of work. The mechanisms are varied: some involve the secretion or absorption of buoyant substances and others a change in the chemical constitution of the body fluids. This article discusses the mechanisms used by a number of creatures, from protozoans and diatoms to whales and sharks.

Claude Bernard [1] advised physiologists wishing to study a particular function to work not on the lower animals but on the higher ones where the function is carried out by a discrete and specialized organ. He argued that although the lower animals possess all the essential properties—such as reproduction, movement, and sensitivity—of the higher ones, you cannot see any sign of the organs that carry out these various functions. 'Herein', wrote Bernard, 'lies their so-called simplicity.'

Our knowledge of the fine structure and the localization of function in small animals has greatly advanced, but Claude Bernard's advice remains sound and his observations on the complexity of simple animals remain true: we can illustrate this particularly well by examples chosen from studies on the buoyancy of aquatic organisms. The proteins, essential constituents of all living cells, are denser than sea water, so that adaptations giving neutral buoyancy, that is giving the same density as that of sea water, will be useful to all levels of marine life. These adaptations are not so much affected by size as are those for other functions such as respiration and movement; thus the ratio of fat to protein for which the lift given by the fat will exactly support the protein remains constant no matter what the size of the animal. We can in buoyancy studies make unusually simple comparisons between large and small animals, for example between squids and protozoans.

In this article we shall divide buoyancy mechanisms into those in which the nature of the solute in the body fluids differs from that in sea water, and those in which fat or gas spaces are used. These we shall discuss in turn, giving as sub-headings the animals chosen for illustration.

The use of body fluids less dense than sea water

Sea water contains about 35 g of salts per kg and has a specific gravity of about 1·026. If an animal could exclude all salts from its body fluids, it would therefore gain about 26 mg lift for every ml of such fluid. The bony fish (the teleosts) often have tissue fluids with less than half the salt content of sea water, and while this is unimportant for the buoyancy of the adults it is probably vital for their eggs. All the commonly marketed marine fishes except the herring have eggs that float upwards in still water; it seems that the yolk sacs of such eggs are impermeable to water, so that the dilute fluids of a parent can be preserved in its eggs and used to give them buoyancy [2, 3]. It may well be that one of the principal advantages to a fish of its dilute body fluids is that of allowing it to lay floating eggs.

The usual disadvantage of having body fluids less salty than the external sea water is that osmotic forces tend to draw water out of the animal, and osmotic work has to be done continuously if the 'watery' body fluids are to be maintained. It is found therefore that most marine invertebrates have body fluids that are isotonic with sea water and that they can gain lift from these fluids only by changing the kind of solutes that they contain. One of the most effective of such changes is that of replacing some of the usual cations of sea water by ammonium ions.

Noctiluca miliaris

As early as 1892, W. C. Goethard and H. W. Heinsius [4] studied the very buoyant and very brightly luminescent protozoan *Noctiluca miliaris* (size about 0·05 cm) (figure 1). They showed that *Noctiluca* is in osmotic equilibrium with the surrounding sea water and concluded that its sap contained an osmotically active substance of lower specific gravity than NaCl. They also showed by qualitative tests that the sap contained ammonia, and attributed the buoyancy of *Noctiluca* to the accumulation of ammonium chloride with a corresponding reduction in the concentrations of other salts. Some later workers have not accepted their conclusions. F. Gross and E. Zeuthen [5] thought it more likely that *Noctiluca* gained buoyancy merely by excluding the heavier divalent ions of sea water. More serious is the fact that T. T. Iida and K. S. Iwata [6] were not able to confirm that *Noctiluca* cell sap did contain high concentrations of ammonium ions. Perhaps these workers caught animals in a different condition, for it is difficult to put any simple interpretation on the results of Goethard and Heinsius other than that which they themselves gave.

Cranchid squids

Recently a quantitative study has shown beyond all doubt that the Cranchid squids do use ammonium ions to gain buoyancy [7]. Three species have been studied; a photograph of a squid of this kind is shown in figure 2. These animals can hang almost motionless in sea water without any apparent effort.

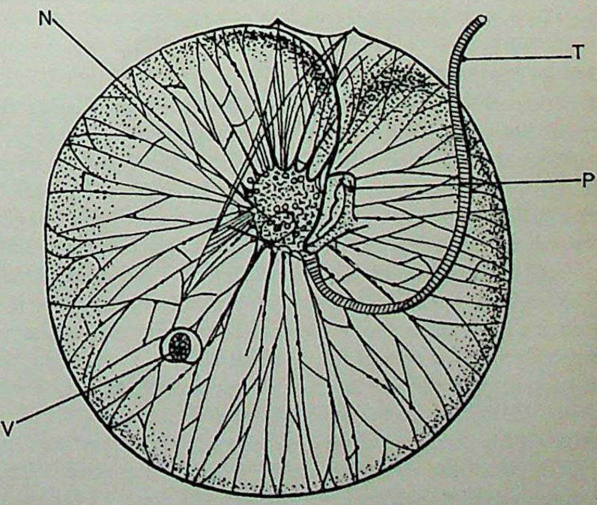

Figure 1 Noctiluca miliaris. *T, tentacle; V, food vacuole; P, central plasmatic mass; N, nucleus (×100) (after Krogh [19]).*

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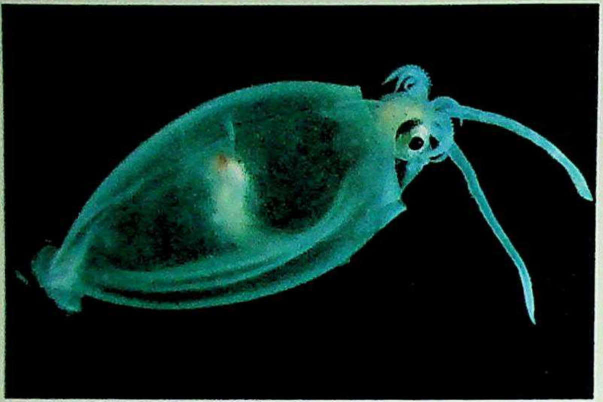


Figure 2 *A cranchid squid* Cranchia scabra. *The outline of the coelomic cavity can be seen through the transparent wall of the mantle. (Photographs 2, 3, and 4 by P. M. David.)*

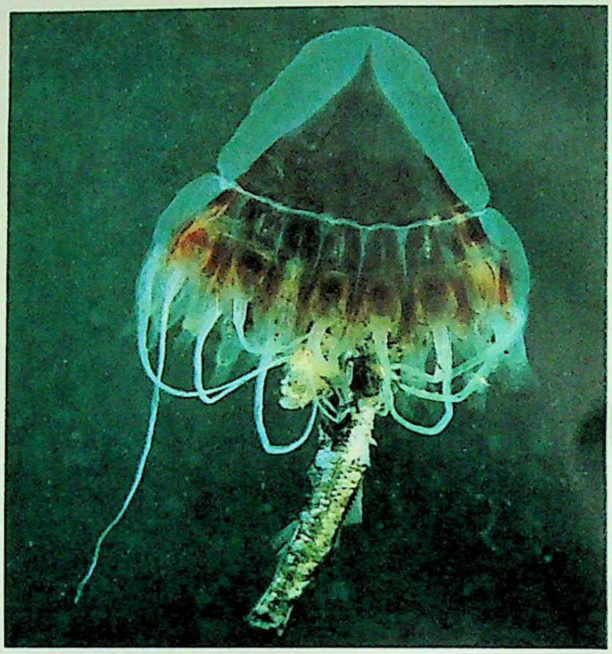


Figure 3 (right) *A deep-sea jellyfish* Periphylla. *The clear jelly-like 'bell' is the principal part that gives lift to the animal.*

When the mantle of such a squid is cut open, an enormous liquid-filled coelomic cavity can be seen. If the membrane surrounding this cavity is punctured, and the fluid it contains drained off, the squid loses its buoyancy and sinks. The coelomic fluids from the several species studied had specific gravities lying between 1·010 and 1·012, and the coelomic fluid accounted for about two-thirds of the weight of each animal. Since the specific gravity of the sea water was 1·026, these animals gained about 16 mg of buoyancy for every ml of coelomic fluid.

Although the coelomic fluids were isotonic with sea water, they nevertheless gave about two-thirds the lift that would be achieved by having pure water as a body fluid. Such low specific gravities could not be given by replacing the 'heavier' ions of sea water with 'lighter' ones, such as replacing sulphate ions by chloride ions. They arise from the extraordinary accumulation of ammonium chloride, the ammonium ion accounting for four-fifths of the total cation content. Ammonia occurs as an end product of protein metabolism, and the Cranchidae have evolved the very neat trick of accumulating their excretory ammonia to give themselves lift.

Ditylum brightwelli

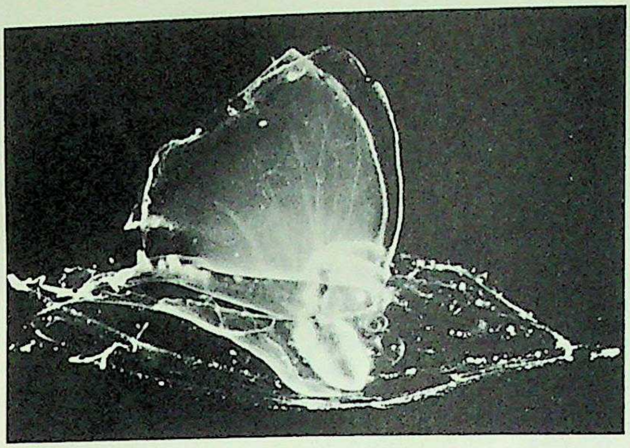
The density of a solution can be altered, while keeping the liquid isotonic with sea water, by changing the relative proportions of the common ions of sea water. If all the other ions of sea water are replaced isotonically by sodium chloride, a lift of about 3·5 mg per ml is given in sea water. Now imagine an animal consisting only of protein and having body fluids isotonic with sea water but containing only sodium chloride. This animal would be neutrally or positively buoyant if it contained less than about 1 per cent protein, and when we remember that a typical fish is about 16 per cent protein, this seems a very ineffective buoyancy arrangement. It may nevertheless be the one most commonly used in the sea.

The diatoms form a very important fraction of the tiny drifting plant life on which all life in the sea depends. They cannot propel themselves; yet they must remain in the upper sunlit layers of the sea if they are to grow and multiply. The regulation of their buoyancy must be of the first importance, and F. Gross and E. Zeuthen [5] have studied the buoyancy of a common diatom, *Ditylum brightwelli* (size about 0·01 cm). They find that under optimal conditions the vegetative cells of this diatom can have the same specific gravity as sea water, while in unfavourable conditions resting spores are formed, with a specific gravity significantly higher than sea water. In the formation of the resting spores, the cell sap that fills the bulk of the vegetative cell is expelled, and Gross and Zeuthen estimate, on the basis of very elegant experiments, that its specific gravity is such that it will give a lift of 2·5 mg per ml in sea water. They suggest that the exclusion of the divalent ions from the sap would account for its lower density. However, it would, at present, be extremely difficult to do chemical analyses on *Ditylum*, and there is no certainty that this very plausible explanation is the correct one.

Recently three Russian workers, C. W. Beklemishev, M. N. Petrikova, and H. J. Semina [8], have succeeded in the astonishing task of analysing the cell sap in single specimens of the giant diatom *Ethmodiscus rex* (volume about 1 mm^3) for Mg^{2+}, Na^+, K^+, Ca^{2+}, Cl^-, and SO_4^{2-}, and they attribute its buoyancy to reduced concentrations of Na^+, K^+, Ca^{2+}, Mg^{2+}, and SO_4^{2-}.

Gelatinous planktonic animals

Here again we find that we can quantitatively demonstrate the use of a mechanism for larger animals. There are very many gelatinous planktonic animals (figures 3 and 4) in the sea, and some of these have recently been studied by E. J. Denton and T. I. Shaw [9]. In all the animals that they studied, and these included medusae (jellyfish), ctenophores (sea gooseberries or comb jellies), heteropod and pteropod molluscs (sea elephants and sea butterflies), and tunicates (or salps), the body fluids had specific gravities less than that of sea water. These body fluids were isotonic with sea water but contained the common ions in different relative amounts. Of these changes in composition, by far the most important in giving lift is the partial exclusion of the sulphate ion. Figure 5 shows how well the buoyancy of the body fluids of these animals can be explained by taking account only of sulphate. Although medusae and ctenophores have sulphate concentrations as low as 40 per cent



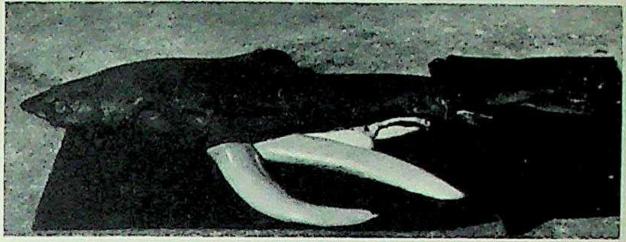


Figure 6 *A Portuguese shark. The abdomen has been opened, and the enormous livers can be seen.*

Figure 4 (left) *A pteropod mollusc (sea butterfly). The buoyant part is the gelatinous skeleton, which is called the 'sabot' of Venus because it is like a small transparent shoe.*

of that of sea water, this will give only about 1·5 mg lift for every ml of body fluid and it can buoy up less than 0·5 per cent of its volume of protein.

The use of fat

Although single-celled animals or plants may exist that use fat as their principal buoyancy device, I do not know of any quantitative study showing this. However, some oceanic copepods have a great deal of fat, and this will undoubtedly bring them much closer to neutral buoyancy than they would otherwise be.

In some fish, such as the mackerel, the amount of fat varies greatly with season; in others, such as the fresh-water eel and the salmon, it varies with the stage in the animal's life. L. Harrison Matthews and H. W. Parker [10], in their general study of the basking shark, have noted that, although the basking shark sinks when dead, the very large fatty liver undoubtedly has an important hydrostatic function. Perhaps the most striking example of the use of fat for buoyancy is provided by some species of shark of the family Squalidae. These sharks have long been known to have very large fatty livers [11] (figure 6), and recently E. D. S. Corner, E. J. Denton, and G. R. Forster [12] have made a quantitative study of the buoyancy of the four species, including the Portuguese shark *Centroscymnus coelolepis* (figure 6).

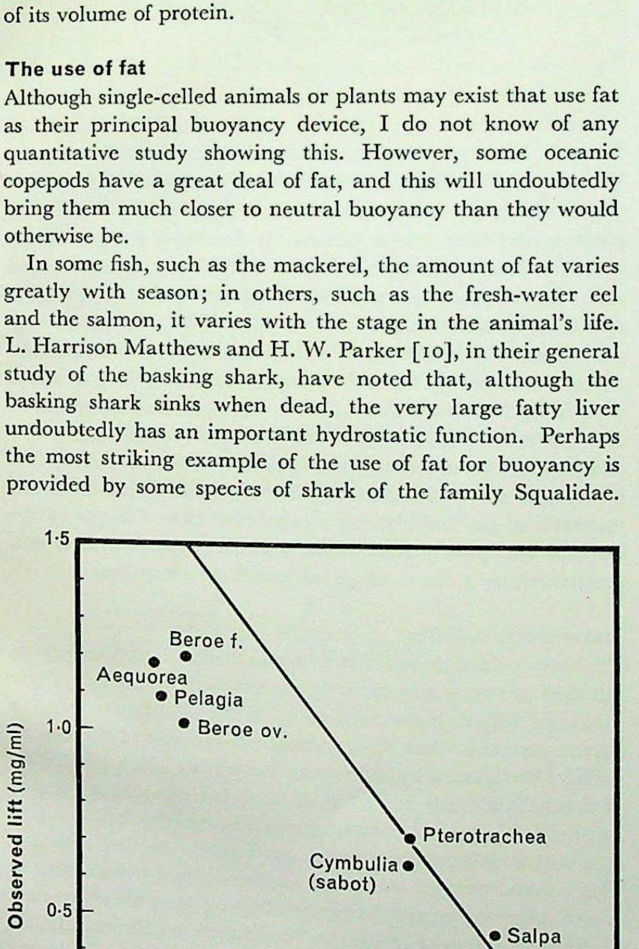


Figure 5 *Observed lift of body fluids in sea water plotted against sulphate concentration. The line shows the lift given for sea waters in which sulphate has been replaced isosmotically with chloride. The abcissa represents sulphate concentrations of body fluids as a percentage of sulphate concentration of sea water [9].*

All the animals studied had enormous livers accounting for about 25 per cent of their total volume, and these livers contained about 80 per cent fat. The livers were clearly the organs that counterbalanced the excess weight in sea water of the other tissues.

The fat of these livers contains very large fractions (sometimes as much as 90 per cent) of the hydrocarbon squalene. Now squalene has the low specific gravity of 0·86, a figure that may be compared with the more typical figure of 0·93 for cod liver oil. This difference in specific gravity does not seem very great, but when we calculate the relative lifts given by 1 gram of squalene and 1 gram of cod liver oil we find that the squalene is about 70 per cent more effective at giving lift. We can at once se the especial utility of squalene for buoyancy, and the probable reason why these sharks accumulate squalene rather than fats in their livers.

Corner, Denton, and Forster [12] have noted that another important group of animals, the deep-diving whales and dolphins, make use of low-density fat to give buoyancy. While the shallow diving whales, such as the blue whale, have fats of density close to that of cod liver oil, whales that dive deeply, like the sperm whale, have large amounts of low-density fats [13]. We can well understand why this is so. Fat gives the blue whale appreciable lift, but since it feeds in the surface waters of the sea on tiny animals and does not normally dive very deeply, the gas space of its lungs must be an important variable in determining its specific gravity. The sperm whale, on the other hand, dives so very deeply that the gas within its lungs must often be compressed to a volume that allows it to give only a trivial lift; the only effective buoyant component is the whale's fat, and the animal clearly gains great advantage in having those fats which will give the necessary lift in the least volume. The low-density fats used by the whales are not hydrocarbons like the squalene used by the deep sea sharks, but esters of long-chain aliphatic alcohols with fatty acids.

The use of gas spaces

Under atmospheric pressure, air has a density only about 0·00125 of that of water, and gas spaces offer the most effective way of giving lift. Animals use two principal methods to maintain gas spaces. In one method, the chamber defining the gas space does not have rigid walls and the gas pressure within the space equals the external hydrostatic pressure. This is the method used in the swimbladders of fish. Since hydrostatic pressure in the sea increases by one atmosphere for every 10 m increase in depth, this may imply large pressures—101 atmospheres at 1000 m depth. The gas pressure will, except at the very surface of the sea, always exceed the combined partial pressures of the common gases dissolved in the sea,[1] so that the gas will have to be actively secreted into the space and some arrangement made to prevent it from simply dissolving in sea water.

The second method is to have a chamber with rigid walls and to pump water out of the chamber. This is the method used in the cuttlebone of the cuttlefish *Sepia officinalis*. The gas within the chamber can now approach equilibrium with the gases dissolved in the sea and its pressure rises towards 1 atmosphere. The rigid wall has to sustain the difference in pressure between the external hydrostatic pressure and the pressure of gas within the chamber.

We might expect that this second method would be the more appropriate for small animals, for it is easy to construct small, light boxes that will sustain compression. It might also be expected that small gas bubbles under pressure would be difficult to maintain because, for a given volume, they would have a relatively large surface area through which the gas could dissolve in the surrounding medium. However, while *Arcella* affords us a clear example of the production of gas under pressure, we have not yet any certain example of use of the second method in a very small animal.

Arcella

Perty first noted in 1849 that the rhizopod protozoan *Arcella* (size about 0·11 cm), which is found in shallow fresh water, can produce gas bubbles in its cytoplasm. Many workers have confirmed his observations, but we owe most of our present knowledge of the buoyancy mechanism of *Arcella* to a paper by E. J. Bles [14].

It is thought that when *Arcella* finds itself in a region of reduced oxygen partial pressure, it forms gas bubbles that allow it to float up towards the surface where the oxygen supply is plentiful. Bles did not generally use reduced oxygen pressure to stimulate the production of gas bubbles, but used the method of reversal discovered by Engelmann. If an *Arcella discoides* is turned over so that it rests on the apex of its siliceous shell, the pseudopodia that protrude through the foramen are directed upwards and can find nothing solid on which to get a footing. Two to fifteen minutes after reversal, during which time the animal seems to make efforts to right itself with its pseudopodia, several dark spots appear in the protoplasm which, over the next 5–20 minutes, swell into distinct gas bubbles (figure 7). The animal then floats to the surface, where it usually attaches itself and creeps away. The gas bubbles now disappear, and if the *Arcella* is detached from the surface it sinks again.

Bles produced strong evidence that the gas involved is principally oxygen. We will describe only two of his ingenious experiments. He soaked *Arcella* for several minutes in rain water to which the vital stain methylene blue had been added, and then washed away the excess stain. The *Arcella* was then colourless, the methylene blue being present in the colourless reduced form. After reversal, the outer zone of protoplasm first became blue, showing that the methylene blue was being reoxidized, and this blue colour then diminished in intensity as bubbles were formed. Later, when the bubbles were disappearing, the blue colour became at first very intense in the cytoplasm surrounding the bubbles and then gradually faded after the bubbles had gone. The whole cycle strongly suggested the production and reabsorption of oxygen. In another experiment Bles made use of a method devised by botanists to detect the oxygen produced by algae. He took a drop of water containing flagellates that had become motionless, introduced an *Arcella*, and showed that these flagellates became active (showing the production of oxygen) only when very close to a reversed *Arcella* that was undergoing the cycle of producing and reabsorbing gas bubbles. Bles concluded that the gas in the bubbles was pure oxygen, and that this was produced and reabsorbed by a chemical action involving an oxidase.

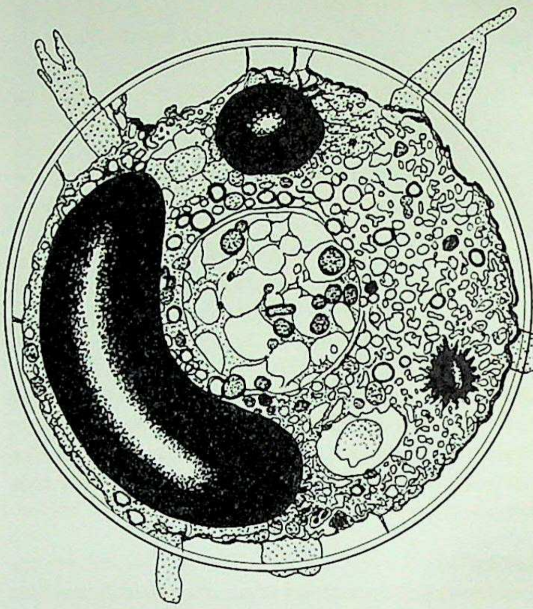


Figure 7 *The protozoan* Arcella *(after E. J. Bles [14]). The large gas vacuoles that this animal can form can be easily seen.*

Tretomphalus bulloides

The truly pelagic foraminifera belong to relatively few species, but they are very important in the economy of the sea. Their shells are the principal constituent of the Globigerina ooze, a marine sediment that covers about one-quarter of the earth's surface. We know very little about the way in which the weight of the shells of these important animals is supported in the sea, but there is a coastal foraminiferan *Tretomphalus bulloides* (size 0·02 cm) which certainly uses a gas float to give it buoyancy. This animal was at one time understandably described as several separate species, corresponding to what we know now as different stages of its life. Its life history, which includes an orderly succession of asexual and sexual generations, has now been clearly described by E. H. Myers [15]. The sexual generation, on reaching a certain size, produces a large terminal chamber containing a gas float, and so converts the bottom living foraminiferan into a free-floating or pelagic animal. On reaching the surface of the sea these pelagic individuals release vast numbers of flagellated gametes that, after pairing, settle to the bottom, where they restart their life cycle.

Here we see the use of a gas float by a very small animal. It would seem more likely that a form that has a solid or firm-walled gas chamber would use the second of our two general methods, but we do not know how the gas space is formed.

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[1] The gases present in sea water are approximately in equilibrium with the atmosphere above the sea, the partial pressure of nitrogen being, for example, at all depths equal to about 0·8 atmosphere.

The swimbladder of the fish

Fish are relatively well studied, and we may content ourselves with a description only of the most striking features of the swimbladder. Many fish, such as the cod and the perch, bring themselves to neutral buoyancy by having a gas space within themselves. This space amounts usually to about 5 per cent of the total volume of a marine fish, and gives a lift that just balances the weight in sea water of the other tissues. The swimbladder wall is not rigid, so that if a fish swims upwards or downwards in the sea and so changes the external pressure acting on it, the gas in the swimbladder either expands or is compressed, and this changes the animal's buoyancy. In response to longer-lasting changes, fish can secrete more gas into the swimbladder or reabsorb gas from the swimbladder so as to restore neutral buoyancy. The swimbladder is used down to astonishing depths—certainly down to 2000 m, and probably down to 4500 m. At this latter depth the pressure will be 450 atmospheres, and the density of the gas itself will demand that the volume be greatly increased if it is to provide neutral buoyancy.

It has been found that whereas the gas from the swimbladders of fish living near the surface of the sea often contains less oxygen than air, the proportion of oxygen increases with depth and gas taken from fish living at appreciable depths is mostly oxygen. It is thus certain that some swimbladders must be capable of secreting oxygen against very steep pressure-gradients. How this is done is not known. The gas is secreted into the swimbladder from a special tissue known as the gas gland. The secretion seems to be intimately linked with the structure called the rete mirabile in which arterioles going towards the gas gland break up into capillaries that come into intimate contact with corresponding venous capillaries arising from the gas gland (figure 8). These capillaries are the longest known in nature, and, as N. B. Marshall [16] has shown in his fine study of the swimbladders of deep-sea fish, the deeper the fish lives, the longer are the capillaries. One species (*Bassozetus taenia*) has retia 25 mm long—a very great length when we consider that the capillaries of muscles, otherwise among the longest found in nature, are seldom longer than 0·5 mm. J. S. Haldane [17] noted that 'This arrangement (the rete) reminds us of that in a regenerating furnace where the heat carried away in the waste gases is used to heat the incoming air.' It is generally believed that in some way gases are 'secreted' from the venous to the arterial capillaries, thus allowing the secreting mechanism to build up, along the length of the rete, an enormous gas pressure difference between the blood in the gas gland and that in the general circulation. The secretion of gas into the swimbladder is clearly the principal problem, for the mechanisms of gas reabsorption are easy to understand. Some fish have a valved duct leading to the oesophagus through which they can allow gas to escape. Others have a structure called the oval, in which some region of the swimbladder wall can be either exposed to or occluded from the gases in the swimbladder by the action of a ring of muscle round its perimeter. This region is served by a blood supply without a rete, and gas can thereby be carried away from the swimbladder when the oval is open.

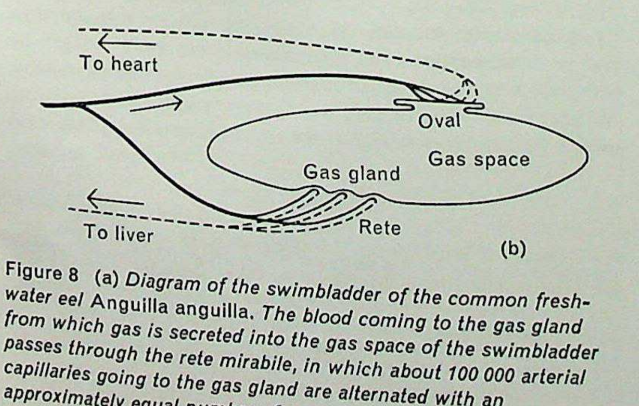

Figure 8 *(a) Diagram of the swimbladder of the common freshwater eel* Anguilla anguilla. *The blood coming to the gas gland from which gas is secreted into the gas space of the swimbladder passes through the rete mirabile, in which about 100 000 arterial capillaries going to the gas gland are alternated with an approximately equal number of venous capillaries carrying blood back from the gas gland. (b) Diagram of the swimbladder of a perch* Perca fluviatilis *(from Prog. Biophys.).*

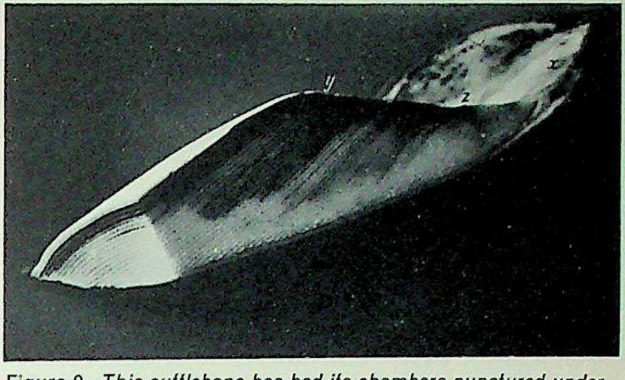

Figure 9 *This cuttlebone has had its chambers punctured under sea water containing ink by a scratch along the siphunclear surface xy. The end has been cut away to allow the lateral penetration of ink to be seen. Ink has been extensively drawn into the newest chambers which contained gas under low pressure. In this figure the cuttlebone is shown ventral side upwards.*

The buoyant shells of cephalopods

Among fossils none are better known or more beautiful than those of the Nautiloids, Ammonites, and Belemnites. The shells of these animals generally served to give them both protection and buoyancy. They are represented today by the shells of such interesting animals as the Pearly Nautilus *Spirula* and the common cuttlefish *Sepia officinalis*. Here we shall describe only the cuttlebone, which has recently been studied by E. J. Denton and J. B. Gilpin-Brown [18].

The cuttlebone consists of a number of thin chambers laid down one below the other at the rate of about one or two a week as the animal grows. The calcareous walls of these chambers are spaced at about 0·7 mm intervals and are held apart by numerous pillars. The whole cuttlebone accounts for about 9 per cent of a *Sepia's* total volume and contains gas spaces that give it a specific gravity of about 0·6 and so allow it approximately to balance the weight in sea water of the rest of the animal. It has been shown that the cuttlefish can vary its specific gravity and that it does so by varying the proportions of liquid and gas space that the cuttlebone contains.

The gas within the cuttlebone is principally nitrogen, and its average pressure is about 0·8 atm, no matter at what depth the cuttlefish is caught. There can therefore be no question of liquid being pumped out of the cuttlebone by gas pressure.

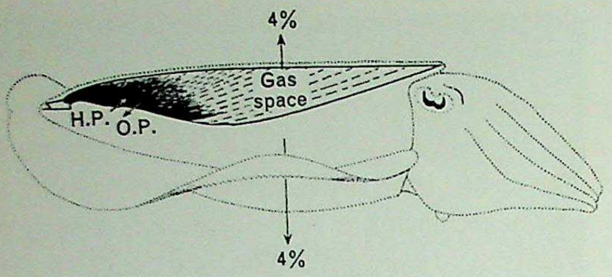

Figure 10 *Diagram summarizing our knowledge of the cuttlebone. The cuttlebone here represented has a density of about 0·6. Liquid within the cuttlebone is marked black. The oldest and most posterior chambers are almost full of liquid. If filled with gas, they would tend to tip the tail of the animal upwards. The newest 10 or so complete chambers, which lie centrally along the length of the animal, are completely filled with gas. These chambers can give buoyancy without disturbing the normal posture of the animal. The hydrostatic pressure (H.P.) of the sea is balanced by an osmotic pressure (O.P.) between cuttlebone liquid and the blood. In sea water, the cuttlebone gives a net lift of 4 per cent of the animal's weight in air and thus balances the excess weight of the rest of the animal. (The black markings in this figure have a quite different meaning from those of figure 9.)*

(Figures 6, 9, and 10 are reproduced by permission of the Council of the Marine Biological Association.)

When a new chamber is formed, liquid is actively extracted, leaving behind a space that contains gas under very low pressure. Gas then slowly diffuses into this space until its partial pressure equals that in the surrounding tissues. This can be shown by a very simple experiment. A freshly dissected cuttlebone is placed under ink and scratched so as to open the posterior edges of its chambers. Ink will now rush into any partial vacuum within these chambers, the extent of the penetration of ink showing the degree of partial vacuum. Figure 9 shows a cuttlebone cut in half at the end of such an experiment. It can be seen that the newest chambers are almost completely filled with ink. This is because the animal has withdrawn liquid so recently from these chambers that very little gas will have had time to diffuse into them; the pressure of gas within them is therefore still very low.

It has also been shown that liquid is pumped in and out only through the posterior ends of the chambers, and we find here a specialized membraen which is thought to do the active pumping. When an animal has been kept in very shallow water, the liquid inside the cuttlebone is isotonic with sea water; in animals just hauled up from the sea bottom it is markedly hypotonic. This does not tell us how the liquid pump works, but it does suggest that equilibrium is maintained by balancing an osmotic force, between the blood and the cuttlebone liquid, tending to extract liquid from the cuttlebone against the hydrostatic pressure of the sea that tends to push water into the cuttlebone. The calcareous structure must sustain the inevitable difference in pressure between the gas inside the chambers and the hydrostatic pressure of the sea. A diagrammatic summary of the functioning of this interesting organ is shown in figure 10.

In this brief survey we have confined ourselves generally to comparisons of large with very small organisms, and we have clearly seen that the elegant buoyancy devices found in higher animals such as the squid and fish have their counterparts in the so-called 'simple animals' such as protozoans. This is a general experience; we have only to recall such things as the astonishingly widespread use in nature of substances like human visual purple and the uniformity in the structure of cilia throughout the animal kingdom to agree with Claude Bernard that the so-called simple animals have not merely the potentialities for evolution into 'higher' ones, but have already evolved the principal functions that the 'higher' ones possess.

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Anomalous patterns in tree rings

W. S. Glock and S. Agerter

It has long been supposed that tree rings are formed annually and so can be used to date trees. The studies of tree-ring formation described in this article have shown that this is not always so, as more than one ring may be formed in a year. However, the results have made it possible to establish a 'tree-ring calendar' by which the timbers of prehistoric buildings can be dated, and they have also shown the way in which micro-climatic changes are recorded in the trees. The patterns of irregularities in the tree-rings are also used in the dating of wood; the results are extremely accurate.

Introduction

Among the first to write about the age of trees were a pupil of Aristotle, Theophrastus of Eresus (c. 372–287 B.C.), and Pliny the Elder (c. A.D. 23–79) [1]. Albertus Magnus (?1193–1280) talked about ring-like layers of wood, and Leonardo da Vinci pointed out that the age of a tree may be determined by counting its rings [2]. Henry Thoreau caught a cold, from which he died, while counting the growth rings on felled timber [3], and even Oliver Wendell Holmes spoke of a 'calendar counted on the rings' [4].

In more recent years, tree rings have been used by A. E. Douglass for dating the Indian pueblos of the American Southwest [5], by J. T. Hack for his studies of the physical environment in the Hopi country of Arizona [6], by E. Schulman to establish a tree-growth index for the Uinta Basin of Utah [7], and by H. S. Colton for dating the last eruption of Sunset Crater in northern Arizona [8]. In Norway, P. Eidem has used tree rings to date numerous buildings and timbers [9].

Characteristics of tree rings

The characteristics of tree rings, particularly as observed in conifers, are as follows. A ring consists of two parts, an inner part that is light coloured, and an outer dark-coloured part. The light wood of the ring has relatively large thin-walled cells; the dark wood has small, radially compressed, thick-walled cells. During a single cycle of wood formation, the first cells set off by the cambium cylinder, the living tissue responsible for the production of both wood and bark in the stem of a tree, are large light-coloured cells. Cells become progressively smaller, thicker-walled, and darker as the growth cycle approaches its end. If wood formation ceases abruptly and completely, the outer boundary of the ring abuts sharply against the light wood of the next outer, younger, ring.

At first sight, tree-ring study is simplicity itself, but complications do arise. Firstly, tree rings are not two-dimensional structures. They are sheaths or layers of wood more or less completely surrounding the trunk, the branches, and the roots, formed in succession outward from pith to bark. 'Growth layer' is really a better term than tree ring, although the latter is in ordinary use.

Secondly, light and dark wood are commonly called spring- and summerwood. These are terms referring to time, and, until investigation proves them to be correct, descriptive terms such as lightwood and densewood are more precise.

Thirdly, the densewoods do not always end in sharp boundaries. Gradations may vary from sharp to diffuse. The lightwood of any single growth layer may even grade outward into densewood, which in turn may grade outward into lightwood. One question arises immediately: if a growth layer ends abruptly at one point in the stem of a tree, must it end similarly everywhere within the stem?

Fourthly, densewoods vary widely in thickness. Some densewoods may be 10–15 cells in thickness, others may have only one cell.

Fifthly, since lightwood is also variable, growth layers may be anywhere from 0·01 mm to 10 mm or more in thickness. A tree in a particular location may have growth layers that are uniform in thickness, whereas a tree in a different location has highly variable growth layers.

Sixthly, the term 'annual ring' implies a precise knowledge of the time of ring formation. It is, however, possible that factors that promote growth may fluctuate within the year as well as annually, depending on the local environment.

Ring variations

The pioneering work on tree-ring analysis in the United States was carried out in the first decade of the present century by A. E. Douglass in the forests of the Southwest, especially in northern Arizona. Douglass, an astronomer, was curious to learn whether tree rings might record weather changes linked with the sunspot cycle. Very soon he realized the complexity of the problem that he had undertaken. Among the obstacles he encountered were the difficulty in finding cycles in rainfall, the complex nature of growth factors, the sometimes hopeless number of cycles in tree growth and other times their complete absence, the variations in the sunspot cycle from 7 to 17 years in the last two centuries, and the lack of knowledge of a uniform, fundamental cycle.

For his purposes, Douglass had to date the rings by counting them inwards from the bark. It soon become apparent that only certain trees from selected locations could be used. Trees away from these locations possessed growth layers too uniform or too variable to be of use for dating purposes. We have extended this work, and have found that in the San Francisco Peaks area near Flagstaff, Arizona, growth-layer characteristics change progressively between trees from high elevations (8000–9000 ft) and those from low elevations (6800–6000 ft and lower), at the border of the treeless arid to semi-arid regions.

Growth rings at the higher elevations are commonly rather thick and strikingly uniform (figure 1); at low elevations near the arid regions, the successive rings in a tree differ greatly in thickness (figure 2). The rings are uniform where the growing season is relatively short and soil moisture is plentiful. High

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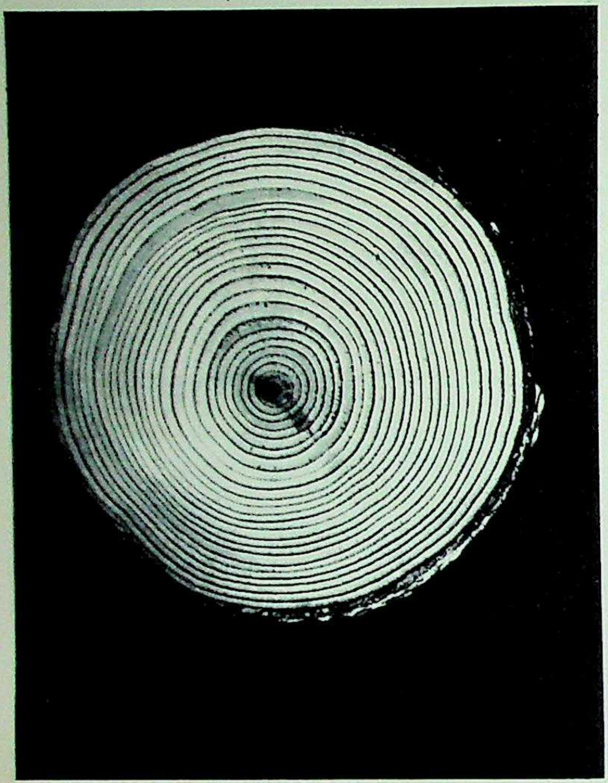


Figure 1 *A ring sequence of remarkable uniformity in ring thickness.*

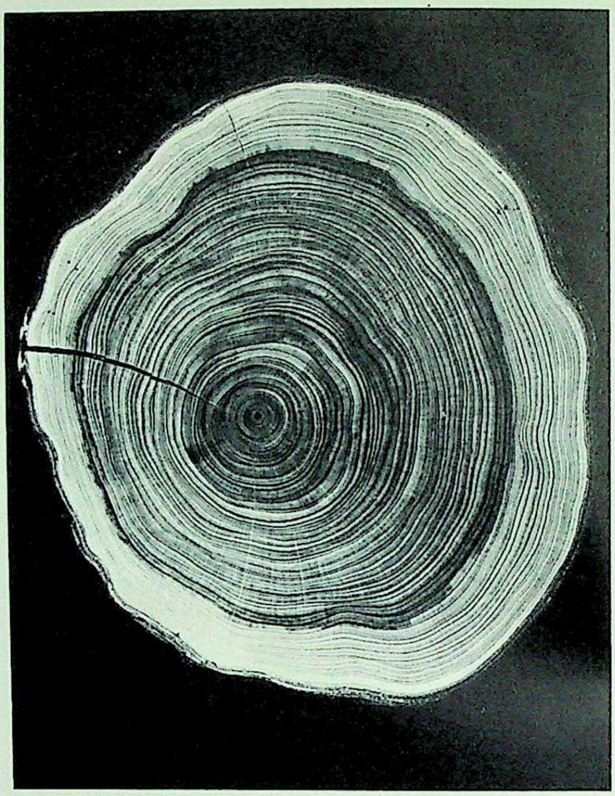


Figure 2 *A ring sequence of great variability and of multiple growth-layers in an annual increment.*

variability occurs where the growing season is long and where large fluctuations of soil moisture occur during that season.

In the region intermediate between the high and low elevations on and near the San Francisco Peaks, ring sequences in the trees are marked by an alternation of groups of uniform rings and groups of variable rings (figure 3). The sequence is said to show moderate variability. It is this degree of variability that makes the pattern of alternating groups of rings so distinctive of the trees growing immediately above the lower forest border. The pattern becomes progressively more subdued toward the forest interior and more variable with the disappearance of the uniform groups toward the arid lands, until, at the very edge of the forest, variability is at a maximum.

Cross-dating

Many people undoubtedly have observed the uncommonly thin and thick rings in Arizona trees, as well as in trees elsewhere in the world. Douglass, however, was the first to use the observations of thick and thin rings for archaeology and climatology. He not only noted the pattern of alternating groups of rings but, and this was important, he was able to trace the pattern from one tree to another. This 'cross-dating' consisted essentially of matching the thin rings and the number of rings between them in a sequence with a like sequence in a second tree (figure 10) [10, 11].

It was found possible to extend cross-dating from tree to tree, into successively older trees, and into beams of structures long since abandoned. A 'master calendar of rings' emerged by the integration of many single ring-records. An unknown sequence in a beam from an Indian ruin could be referred to this chart, cross-dated, and assigned a calendar date which, although conceivably in error by half a dozen years or so, had a remarkable degree of accuracy.

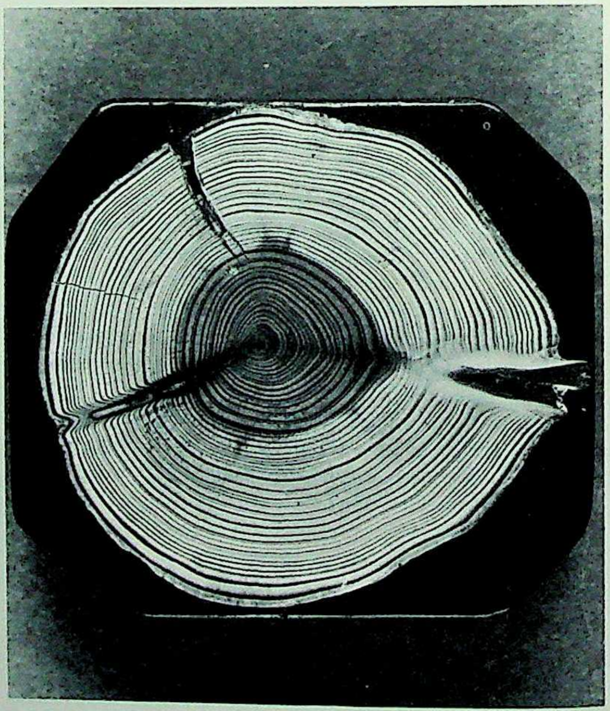


Figure 3 *A sequence combining certain features of high- and low-altitude rings. Note the succession of uniform and variable rings. In trees such as this, cross-dating is at its best.*

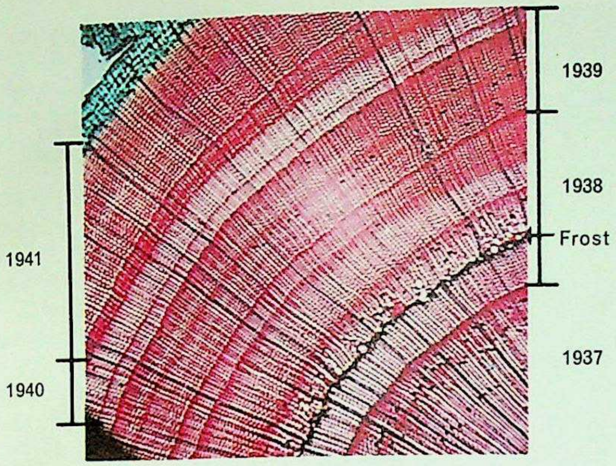

1939
1938
Frost
1937
1941
1940

Figure 4 Cupressus arizonica, *cut 27th June 1941. This shows frost injury and recovery in 1938, and multiple growth-layers.*

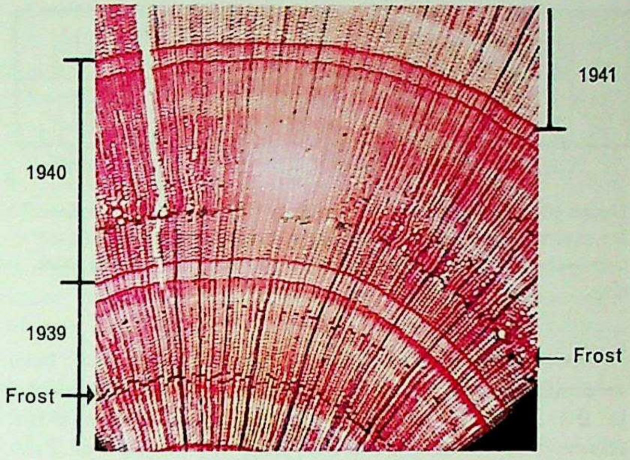

1941
1940
1939
Frost
Frost

Figure 5 Cupressus arizonica, *cut 29th November 1941. An excellent example of multiple growth-layers.*

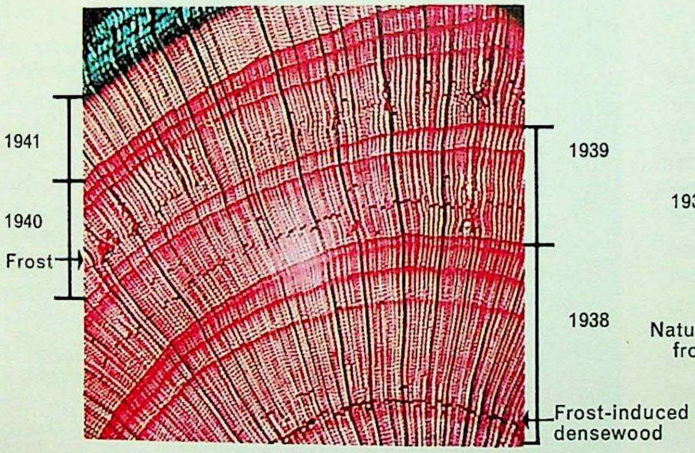

1941
1940
Frost
1939
1938
Frost-induced densewood

Figure 6 Cupressus arizonica, *cut 11th October 1941. Note the regular succession of thin growth-layers.*

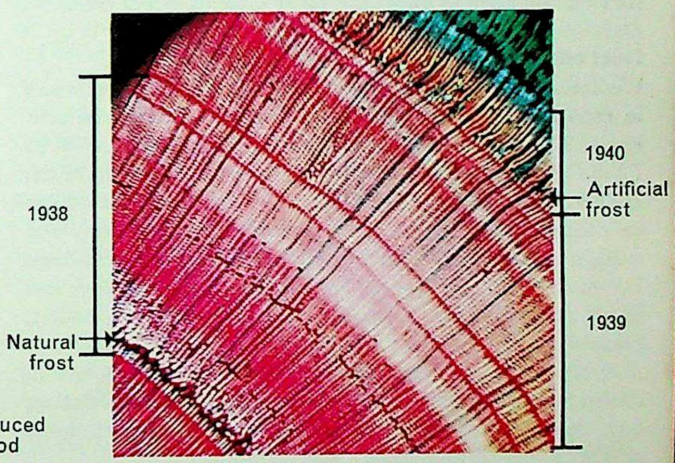

1938
Natural frost
1940
Artificial frost
1939

Figure 7 Cupressus arizonica, *cut 10th May 1940. 1940 shows vivid example of the effects of artificial frost applied 8th April. Recovery cells and normal xylem formed before 10th May.*

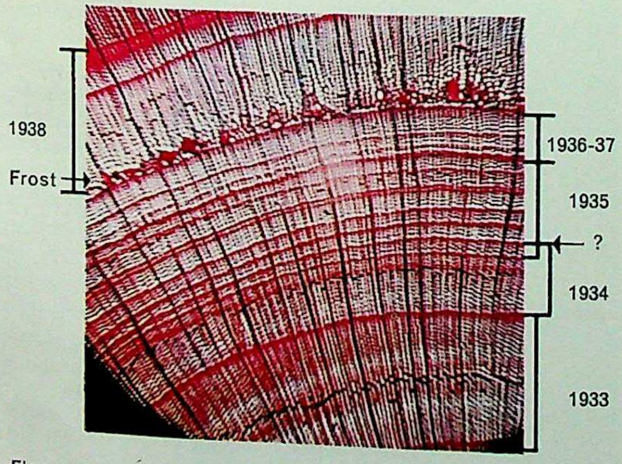

1938
Frost
1936-37
1935
?
1934
1933

Figure 8 Cupressus arizonica, *Texas Agricultural Experiment Station. A treasured section in tree-ring studies and a marvel of cambial activity, differentiation, maturation, and multiplicity. Absolute dating by means of natural frost effects and by their absence in 1935.*

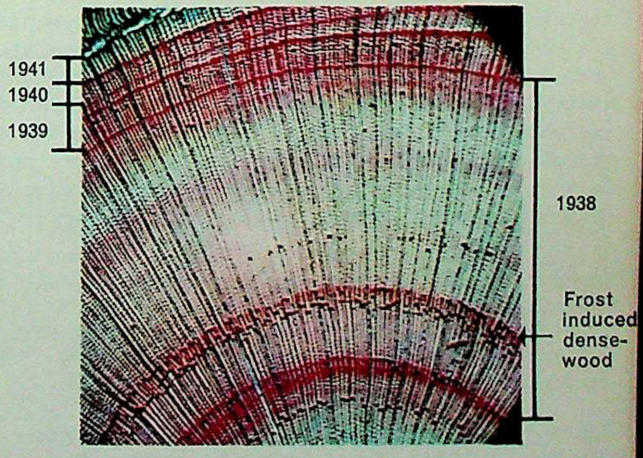

1941
1940
1939
1938
Frost induced dense-wood

Figure 9 Cupressus arizonica, *Texas Agricultural Experiment Station, cut 20th August 1941. Example of frost-induced densewood and multiplicity. 1938: physiological shock of low temperatures induced densewood formation instead of disruption of the cambium. 1941: Incomplete; cambium dead, killed by artificial freezing 9th May 1941.*

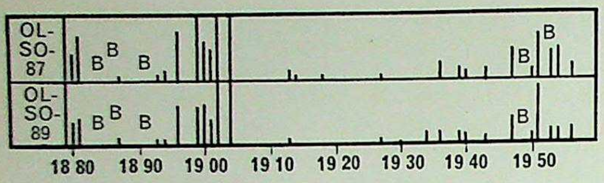


Figure 10 *Cross-dating. The two trees* (Pinus ponderosa *Laws.*) *are separated by more than 100 yards. Inked lines represent thin rings—the thinner the ring, the taller the line. B refers to a thick ring.*

Tree-ring analysis and the master calendar have been successfully used in dating many Indian structures and pueblos in the American Southwest. Objections to the supposed accuracy of prehistoric dates have been raised, but, even if the accuracy is not as high as was at first supposed, it goes far beyond that of any other known method. Errors ranging from zero to 10 per cent have been suggested, averaging less than 5 per cent. In comparison, wood of known date subjected to radiocarbon analysis gave an error of close to 20 per cent.

Frost effects

We have said that maximum variability occurs in ring sequences in trees at the extreme lower forest border, next to the arid lands. A fortunate opportunity came in 1938 to one of us (W.S.G.) when he moved to Lubbock at the south end of the High Plains in West Texas. Here, indeed, lower forest border conditions existed. Trees grew naturally in the gullies and shallow canyons along the Break of the Plains eastward from Lubbock. On the campus of Texas Technological College and on the grounds of the Texas Agricultural Experiment Station, planted trees were used for experimental purposes. These experiments led to the recognition of natural frost injury as a dating instrument. They also gave a method of absolute dating, and demonstrated the existence of multiple growth-layers within an annual increment.

During the winter of 1938–39, stained thin sections were made from different trees, from different branches of the same tree, and from different parts of the same branch. A first glance at the sections under a microscope revealed a severe injury followed by distorted cells near the interior of the outermost, 1938, increment (figure 4). Growth for 1938 thus gave the following succession, recorded from the cells first formed out to the inner bark. There were four to six normal xylem cells; a rope-like structure made of collapsed cells; grossly distorted and enlarged cells which gradually gave way outward to normal cells; and the resting cambium. The injury and recovery were recognized at once as an excellent example of the frost rings described and illustrated by I. W. Bailey [12].

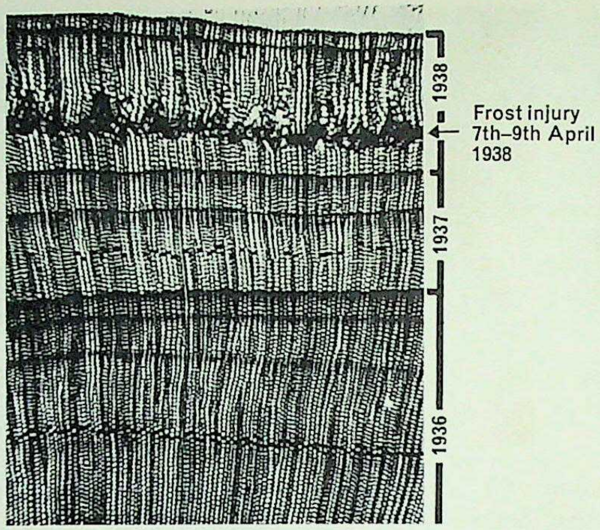
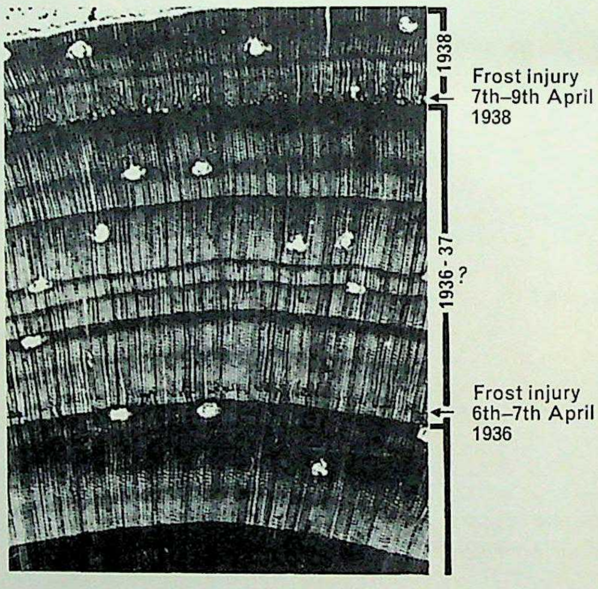
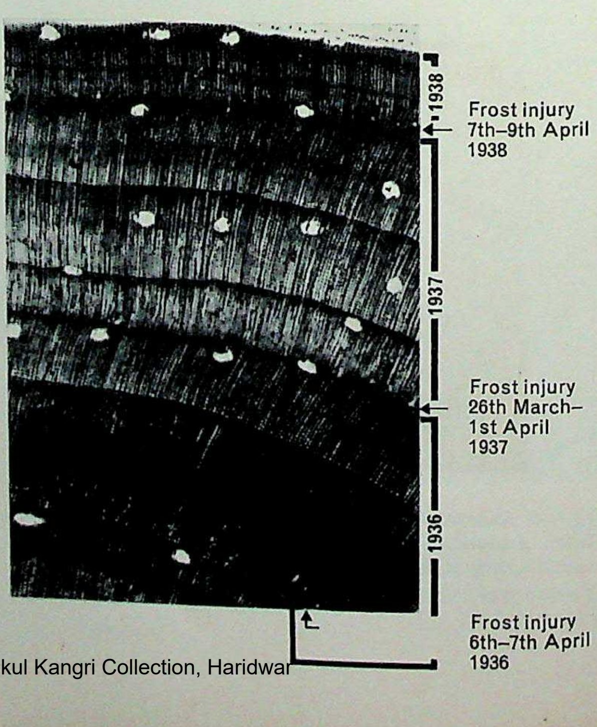


Figure 11 (top right) *Arizona cypress* (Cupressus arizonica *Greene). This shows the frost injury and recovery of 7th–9th April 1938. Frost effects were identified in wood of 1937 and 1936. The annual increments of 1936, 1937, and 1938 have two sharply demarcated growth-layers each.*


1938
Frost injury 7th–9th April 1938
1936-37 ?
Frost injury 6th–7th April 1936


1938
Frost injury 7th–9th April 1938
1937
Frost injury 26th March–1st April 1937
1936
Frost injury 6th–7th April 1936

Figures 12 and 13 (centre right, and bottom right) *Ponderosa pine* (Pinus ponderosa, *Laws.*). *Sections from two branches. Both photographs show 5 growth-layers between the frost effects at the start of 1936 and at the start of 1938. However, it is not clear in figure 12 which layers belong to 1936, and which to 1937. Figure 13 solves this problem. It shows the effects of a mild frost at the start of the third growth-layer out from the start of 1936. This is the frost of 1937 which thus assigns two growth-layers to 1936 and three to 1937.*

By its position, the injury indicated the effects of a late spring frost. Weather Bureau records and damage to foliage revealed that killing frosts did occur during the nights of 7th, 8th, and 9th April 1938. An unusually warm March had caused the initiation of cambial activity and the formation of xylem four to six cells deep radially. Then the sudden drop in temperature in April ruptured the cambial derivatives and they collapsed, forming a dark, irregular, rope-like zone of injury. After the injury, the additional cells gradually returned to normal as the cambium set off successive cells radially outward.

The effects of the 1938 frost were first identified in thin sections from Arizona cypress (*Cupressus arizonica* Greene), where they were most intensely and almost universally recorded. Later search revealed frost effects, more or less subdued, in fourteen additional species.

With the identification and dating of the 1938 frost effects, which typically were intense and usually some distance outward in the year's growth, it was realized that here was a method providing an absolute date. The frost, by placing a tag within the wood, had provided a check point in time.

Multiple growth layers

The study of thin sections had scarcely begun when a new phenomenon was discovered. A thin growth layer had appeared under the cambium at the outside of the 1938 xylem. The thin sections showing this second growth layer in 1938 were taken from the same branch, a few centimetres from those that showed only one growth layer for 1938. Indeed, two growth layers, one thick, the other thin and lenticular, proved to be more common than one growth layer in this particular annual increment. Three growth layers, in fact, were not unusual. A maximum number of five growth layers was discovered in the trunks and branches of two trees, one tree on the campus of Texas Technological College and the other five miles distant at the Texas Agricultural Experiment Station (figure 8). It must be pointed out that these intra-annuals were as distinctly developed and as sharply defined on their outer margin as any single annual increment. Without frost effects as a guide, attempts at exact dating of xylem formation would have been futile. The thin sections on which frost injury was first noted and which led to the discovery of multiple rings are shown in figures 11–13.

However, the idea that a tree may grow more than one ring a year is not new. For instance, in 1887 R. W. Furras in Arizona cited proof that rings are not annual [13]; in 1893 C. Abbe, reporting on the work of J. Keuchler, stated that 'in Texas two quite distinct periods of growth and repose' have been observed within one year [14]; and in 1912, H. P. Brown found many double rings in New York trees [15]. C. G. Dobbs, who studied over 100 sections of larch in a 50-mile radius round Bristol, England, found double rings so common that he used them for cross-dating [16]. In contrast, I. Hustich and J. W. Marr gave strong evidence for unity of the annual increment in trees on the east coast of Hudson Bay [17, 18].

The next problem was to distinguish annual growth-layers from intra-annual ones. The study of frost injury and recovery in West Texas trees over a span of years provided the answer [19].

Natural frost had given a method of precise dating; it was only logical, therefore, that, because of its adaptability and timing, the use of artificial frost should be considered. An apparatus was devised late in 1939 to produce low temperatures by the use of solid carbon dioxide [20].

It was found to be possible to produce an internal marker in the newly formed cells by artificial freezing (figure 7). Only within certain rather strict physiological limitations, however, is it possible to use artificial freezing with success. It is unsuccessful if freezing is applied too soon or too late in the spring, as mature cells do not readily lend themselves to distortion and collapse. The spectacular results of frost injury and recovery, as shown in the illustrations, can be produced only in newly formed cambial derivatives whose cell walls have not yet hardened.

Ten years of observations, measurement, and experimentation with trees from the lower forest border, using both natural and artificial frost to produce exact dating, gave ample evidence of multiple growth-layers within an annual increment (figures 5, 6, 9). Cambial activity is a highly complex affair that depends in part on the fluctuations in available soil moisture during the growing season. If soil moisture is plentiful, cambial activity in cell divisions tends to be continuous and to produce one fairly large growth-layer for the year. If the soil moisture is depleted early in the season, cambial activity in cell division ceases, and densewood forms. This may or may not complete the annual increment. If the soil moisture is replenished during the growing season, cambial activity may be re-initiated and a second growth layer will be formed. This initiation and cessation may occur several times within one year's growth.

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The organization of enzyme biosynthesis in yeast

Alan Wiseman

The living cell can sometimes synthesize enzymes, in addition to its normal ones, when it has to metabolize particular compounds that it has encountered. The 'information' required by the sites of protein synthesis is thought to be carried in 'messenger' ribonucleic acid from the genes. It seems that it may soon be possible to intervene in this process, and thus direct the cell to synthesize enzymes catalysing a specific series of reactions. This article discusses the mechanism of the production of enzymes in yeast and suggests the lines of future progress in study of this mechanism.

Yeast cells are capable of using simple nutriments to build up the complex substances required for the maintenance of their structures as well as for growth and reproduction. The ultimate nutriments necessary are, however, less simple than those utilized by green plants, which in the presence of sunlight need only mineral salts, water, and carbon dioxide. Lacking chlorophyll, yeasts, like most other non-green micro-organisms, cannot make use of the energy of sunlight to produce the sugars they require. Instead, they need these or other energy sources to be provided in their growth medium, often along with the amino acids, traces of certain metals, and vitamins of the B-complex.

The amino acids are required for making proteins, which consist of long chains of these units; some twenty different amino acids are involved. The sugars are largely employed to obtain the energy needed for this process. The proteins are of great importance to the yeast cell, as to life in general, because they often constitute enzymes, that is, specific catalysts for reactions which otherwise would occur either only slowly or not at all. In yeast, as in most other organisms, the synthesis of proteins that serve as enzymes takes place by a series of complex chemical reactions under the influence of already existing enzymes, and so the process is self-perpetuating. The first step of one widely occurring route involves the activation of the amino acids inside the yeast cell. This process puts the amino acids into a high-energy state, ready to be moved to the site of protein synthesis and joined together. The activator is adenosine triphosphate, which is produced by the yeast cell, using the energy derived from the breakdown of sugars, such as glucose and maltose, present in the growth medium. This substance contains the energy of the split sugar molecules trapped in its energy-rich phosphate bonds, and it is capable of donating this energy, in the presence of the correct enzymes, to each of the amino acids. The activated amino acids are then transported to the site of protein synthesis in the cell by combination with soluble ribonucleic acid (see below).

The specificity of enzymes depends upon the variety of amino acids present in the chain, the sequence in which they are arranged, and the way in which the chain is folded. The synthesis of a particular protein therefore requires that its constituent amino acids be arranged in a specific order. Recent theories postulate that the site of protein synthesis in the cell is capable of doing this because it continually receives information about the correct sequences of amino acids from the ultimate controller, or gene, situated on the chromosomes. In general, the chromosomes determine the heritable characteristics of the cell: one gene is considered to determine the structure of one enzyme by organizing the site for its synthesis. A 'messenger' ribonucleic acid carries the necessary information from the nucleus to the site of synthesis, the message being encoded in the sequence of its long chain of constituent nucleotides (phosphate-sugar-bases). As both the building site (the microsomes) and the messenger material are ribonucleic acids (RNA) and since the gene is of a substance with some similar features (deoxyribonucleic acid, DNA), the nucleic acids obviously play a vital role in the life of the cell.

It is further postulated that the activated amino acids, now correctly arranged, are joined together by further enzymatic reactions and that the long chains are folded in a specific manner to yield the final protein. The finished enzyme is capable of catalysing specific chemical reactions in the cell, perhaps even assisting in the synthesis of its own kind of molecule. Thus the cyclic processes continue, allowing the yeast cell to grow, reproduce, and effect all the delicate chemical transformations that constitute life.

Control of enzyme synthesis

Although yeast cells can grow and divide in a medium containing glucose as the sole source of energy, these processes are temporarily halted when maltose, a sugar whose molecule consists of two units of glucose, is substituted for the monomer. After a characteristic interval, maltase, the enzyme required to metabolize the added maltose, begins to be produced and so growth and division are renewed. This induction of the synthesis of a particular enzyme is one aspect of the adaptation of the yeast to its new environment. The induced enzyme is, however, lost again on prolonged contact with a medium lacking maltose. It would, therefore, seem that the yeast cell is capable of producing the enzymes it needs to metabolize the sugars with which it is in contact. However, although, for example, the disaccharide cellobiose induces the formation of the β-glucosidase that degrades it to usable fragments, other sugars are known to induce the appearance of this enzyme even though they cannot be broken down by it [1, 2]. It is apparent that, because of imperfections in the controlling mechanisms, yeast can produce enzymes that are not necessarily beneficial to its chance of survival.

The phenomenon of induced enzyme formation in yeast has been shown to result from the synthesis of entirely new protein rather than by activation or modification of an existing enzyme. For example, no adaptation occurs unless those amino acids which are required for the new protein and which cannot be made by the yeast from other nutriments, are present [3]. The quantitative incorporation of radioactively labelled amino acids into the induced enzyme during induction has been demonstrated [4, 5], affording a satisfactory proof of this hypothesis. Induced enzyme synthesis therefore represents a synthesis of protein that can be studied with relative ease, because it occurs prior to renewed growth, with its resulting complexities, and

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gives a readily identifiable product. In appropriate circumstances, the amount of protein formed can be assessed by measuring how much of the products of its enzymatic reaction are formed. For example, maltase can be estimated by measuring the quantity of glucose produced by its action on maltose.

The mode of action of the inducer is of considerable interest. It is well known that although the presence of a little glucose as an initial source of energy stimulates adaptation, higher concentrations of glucose inhibit, for example, the synthesis of β-glucosidase. There are several possible explanations of this glucose effect. The simplest is that it is the result of preferential use of the immediately available glucose, rather than of glucose formed by degradation of the disaccharide; this would involve the prior synthesis of the relevant enzyme. One of the chemical mechanisms concerned in the phenomenon involves the prevention by the glucose of the release of the newly synthesized β-glucosidase [6]. This enzyme is immobilized because it remains bound to the building site in the microsomes; it is active only in solution in the cell cytoplasm. Alternatively, the explanation may lie in repression by the glucose of the genic controlling unit that normally forms the messenger RNA necessary for producing the enzyme required for the release of the newly synthesized β-glucosidase from the microsomes. It then follows that enzyme induction is due to the removal by the inducer of an inherent repressor. In the absence of the inducer, this repressor prevents the synthesis of the particular messenger ribonucleic acid required for the production of the corresponding protein [7, 8].

It is thought that the repressor may contain RNA [8]. As it is well known that inducers can combine with their enzyme, even though they may not be attacked by it, it is conceivable that the enzyme and its messenger RNA are enzymatically linked to form the repressor. It is possible that this substance does not combine with certain non-inducers, even though these are capable of complexing with the enzyme itself. If this were so, only the inducer could continuously remove the repressor from the gene by means of its binding ability. This hypothesis is supported by the observation that inducible enzymes are usually present, although in small quantity, in inducible strains before induction [2]. They could be bound to genes, and repress the synthesis of more of the enzyme.

Another way of control of enzyme production by the cell involves the inhibition of certain metabolic pathways by a product of the series of reactions involved. This type of control has the nature of a 'feedback' mechanism in which the final product of a multistage process inhibits the enzyme controlling an earlier one, usually the first. This feature of the system ensures that no unwanted intermediates accumulate.

It must be emphasized that the many enzyme reactions occurring in the normal cell work in a coordinated way, even though this coordination is achieved indirectly by stimulation and repression, as previously discussed. The ultimate controllers, the genes, generally form part of the chromosomes. These long chains of DNA molecules have an inherent chemical code represented by the sequence of the monomer units (nucleotides) constituting the macromolecules. Proteins are formed in accordance with this code by the chemical mediation of messenger RNA molecules. These relatively small units are synthesized as a replica of small segments of the chromosomes, the genetic information therein being transferred to the microsomes [9].

Pathways of protein biosynthesis

Having briefly discussed the control of enzyme synthesis, there remains the question of the cellular technique involved in activating and collecting the required amino acids in the correct order at the sites of protein synthesis.

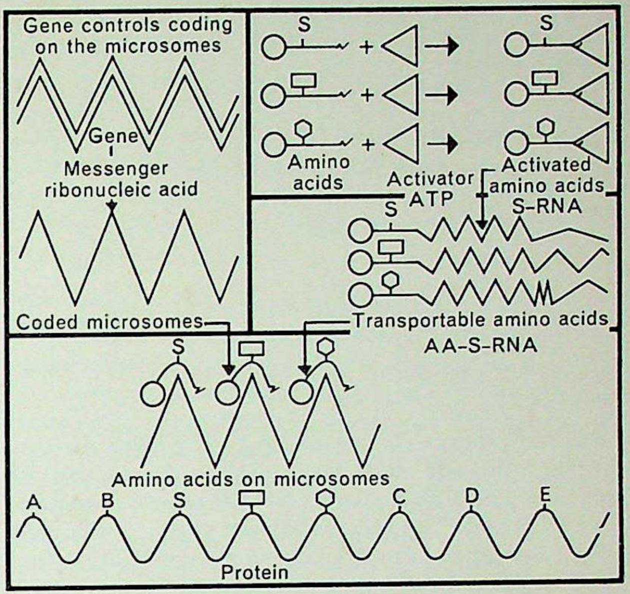

Gene controls coding on the microsomes
Gene
Messenger ribonucleic acid
Coded microsomes
S
+
Amino acids
Activator ATP
Activated amino acids S-RNA
Transportable amino acids AA-S-RNA
S
Amino acids on microsomes
A
B
S
C
D
E
Protein

Figure 1 *The classical scheme for the genetically controlled biosynthesis of enzymes.*

Figure 1 illustrates a general pathway for the activation of amino acids and their genetically controlled incorporation into proteins. This sequence of reactions is known to occur in yeasts as well as in other micro-organisms, and in plant and mammalian cells [10]. The first stage, activation, consists of the combination of each of the twenty amino acids (AA) with adenosine triphosphate (ATP); this is accompanied by elimination of a pyrophosphate group (pp) and formation of a complex of amino acid, adenosine monophosphate, and enzyme, AA–AMP–E:

$$\mathrm{AA + ATP + enzyme \rightleftharpoons AA\text{–}AMP\text{–}E + pp} \quad \ldots.(1)$$

The activated amino acid remains firmly bound to the enzyme until it reacts with the soluble ribonucleic acid (s-RNA):

$$\mathrm{AA\text{–}AMP\text{–}E + s\text{-}RNA \rightleftharpoons AA\text{–}s\text{-}RNA + AMP + E} \quad \ldots.(2)$$

It is thought that in a given organism, each amino acid requires only one enzyme for these reactions, and each seemingly reacts only with a specific type of soluble ribonucleic acid.

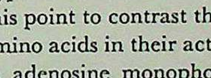
It is necessary at this point to contrast the mode of chemical combination of the amino acids in their activated states. When in combination with adenosine monophosphate (AMP) the amino acid is joined to the phosphate by the highly reactive phosphoanhydride bond, which can be represented as

Adenine ribose phosphate ~ AA

On transfer to the soluble-ribonucleic acid the link is changed to the somewhat less reactive ribose-ester bond:

Adenine ribose ~ AA

in which the amino acid is joined to the terminal adenine-ribose unit of the polymeric soluble-ribonucleic acid. In each case the amino acid is combined through its carboxyl group,



$$\ldots\mathrm{OOC{-}\underset{\displaystyle R}{\underset{|}{C}H}{-}NH_2}$$

Returning now to the next stage in the synthetic process, the transferable amino acids (AA–s-RNA) are moved to the microsomes, where they join together to form proteins; it is not certain whether other intermediates are involved in this

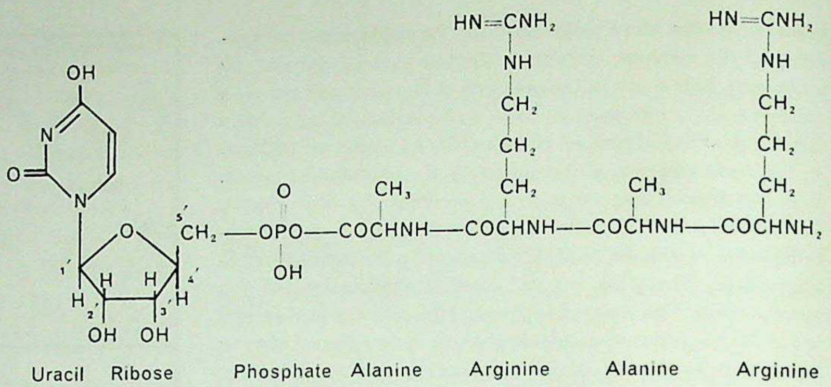


Figure 2 *Arginylalanylarginylalanyl-5′-uridylate, the first peptidyl-nucleotidate isolated from yeast.*

particular pathway. It was usually assumed that the hundreds of amino-acid molecules required for the synthesis of a particular protein molecule were laid down on the microsomal ribonucleic acids. The high energy state of these amino acids allows them to be joined together on the genetically defined ribonucleic acid template in the correct order for the synthesis of the specified protein.

An 'adaptor' hypothesis has been put forward. It is sometimes supposed that an 'adaptor' RNA is formed along with the template RNA on the same deoxyribonucleic acid template in the chromosome. The small adaptor ribonucleic acids might be fragments of s-RNA, which as a whole may be too large for the adaptor function. The fragments could carry their respective amino acids to the positions on the microsomal template ribonucleic acid corresponding to an identical sequence of their constituent nucleotides. This hypothesis is an attempt to overcome the conceivable coding difficulties of arranging twenty amino acids in a predetermined sequence on the microsomal template, recognition of the correct sites being left to the adaptor ribonucleic acids rather than to the amino acids. A slight modification of this theory has become necessary since the discovery of messenger ribonucleic acid, for it has been realized that the microsomal template ribonucleic acid may be only an inert carrier of the genic message delivered by this fraction. It is precisely the continual synthesis and delivery of this transient message from the gene that allows the very rapid take-over of the bacterial cell metabolism by the viruses (bacteriophages) that are known to attack bacteria [11] (see below).

The final stage in protein biosynthesis on the microsome involves the release of the completed polypeptide from the template; this process also has been shown to require ATP as well as certain cofactors and an enzyme [12]. The liberated polypeptide chains can now assume their characteristic three-dimensional configuration.

The now classical pathway to proteins, the essentials of which are described above, is by no means the only such route. Microsome-like particles (ribosomes) also occur, it seems, in other parts of the cell, such as the nucleus, where analogous means of protein synthesis have been demonstrated. In addition, the cell structures known as mitochondria, the sites of cellular respiration, also synthesize protein, perhaps by entirely different routes.

In yeasts, one possible route involves peptidyl-nucleotidates, which are widely occurring compounds possessing the chemical characteristics of both protein and nucleic acid. The peptide and nucleotide moieties are joined together by either anhydride or ester bonds, as described for the amino acid adenylates (AA–AMP) and soluble-ribonucleic acid esters (AA–s-RNA). The peptidyl-nucleotidates are thought to be intermediates in protein biosynthesis and even perhaps in ribonucleic acid synthesis. Alternatively, they may be involved in the synthesis of the microsomes themselves, as these contain protein and ribonucleic acid. On the other hand, some of them may be formed by the partial degradation of existing proteins with recyclization of these activated fragments into new protein, perhaps in the form of adaptive enzymes [13]. Short-lived messenger RNA may itself break down with the simultaneous activation of microsome-bound peptides to form some peptidyl-nucleotidates which may later form protein. A more detailed account of these important compounds is given in the following section, where an attempt is made to elaborate some of these possibilities.

Peptidyl-nucleotidates and protein biosynthesis

Two simple examples of this type of compound have so far been conclusively identified by degradation and synthesis (for review see [14]). One is a tetrapeptide-nucleotidate anhydride (figure 2) and the other an amino-acid–dinucleotidate anhydride (figure 3). Many more such compounds, of diverse composition, have been isolated from brewers' yeast, although their structures have not been fully elucidated. All contain a variety of peptides formed from several amino acids joined to part of a ribonucleic acid molecule by either an anhydride or an ester bond [15, 13]. It has not yet been conclusively established that the esters are s-RNA derivatives. Examination of the peptide moieties has shown that the anhydrides always contain an excess of the basic amino acids, and most of the esters also show this feature. The result of this combination is that the compounds can show an overall positive charge in spite of their acidic nucleotide content. The further metabolism of these materials might depend on this feature as a prerequisite for their combination with an acidic nucleic-acid template. These compounds could then be joined together to produce proteins and perhaps ribonucleic acid. Tracer studies with radioactive arginine have shown that it is absorbed from the nutrient medium by yeast and later appears successively in the peptidyl-nucleotidate fraction and in protein. The passage of the labelled arginine in this direction indicates that these activated compounds are intermediates in protein biosynthesis in yeast [16].

Further studies [13] have revealed that the relative amounts of esters and anhydrides extracted from the yeast depend upon the age of the yeast culture when its biochemical equilibrium was stabilized by rapid freezing. If yeast is inoculated into a large excess of nutrient medium it soon begins to multiply by division. In these circumstances, of the two types of activated compound, only peptidyl-nucleotide anhydrides are present. Growth eventually abates due to the depletion of nutriments and the accumulation of inhibitory end-products. In this late phase of growth the esters constitute half the total nucleotide-peptide material. It is well known that, in the absence of sufficient nutriments, micro-organisms degrade some of their

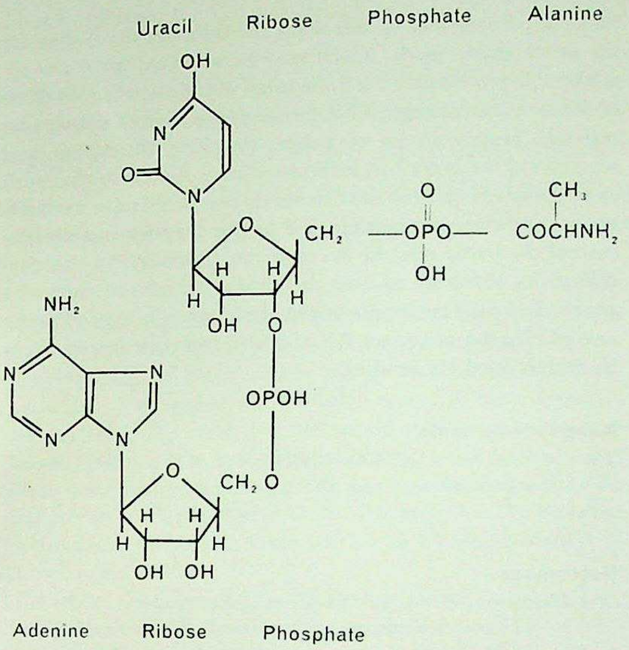


Figure 3 *Alanyl (3′-[5′-adenylyl])-5′-uridylate.*

proteins in order to form the enzymes necessary for their survival. It seems possible that under these conditions some of the esters formed may represent the intermediates in this recyclization of proteins. The esters, although activated, are at a lower level of chemical energy than the anhydrides, and are therefore the more economical intermediates. An alternative explanation is that both esters and anhydrides are intermediates in the *de novo* synthesis of proteins, but that the esters accumulate in the yeast cell only in the later phases of growth, because there is then insufficient energy available for them to be further metabolized. S-RNA-peptide esters are in fact conceivable intermediates in the classical pathway, where they could be formed by the stepwise elongation of the microsome-bound peptide chain which remains attached to an s-RNA molecule. Another feature of yeast growth is that only about one-third of the anhydride material is present in the later phases of growth, as compared with the earlier phases. This result is in agreement with the idea that the anhydrides are also involved in some synthetic processes, for rapid synthesis of microsomal protein occurs at this early stage.

We have now isolated the enzymes concerned in the formation of some of these compounds, and an investigation of the system is in progress. Both esters and anhydrides are formed from peptides; figure 4 illustrates a conceivable relationship between amino acids, peptides, and proteins. Peptides could have been formed from amino acids by another enzyme system, or absorbed intact from the nutrient medium (exogenous peptides). It is likely that these investigations will help to show how enzyme biosynthesis in yeast is controlled at various stages in the growth cycle; the pathways studied in these investigations may well be of general occurrence. Similar mechanisms for protein synthesis appear to exist in all organisms, although several routes may be used concurrently, the dominant pathway at any time depending upon the prevailing conditions.

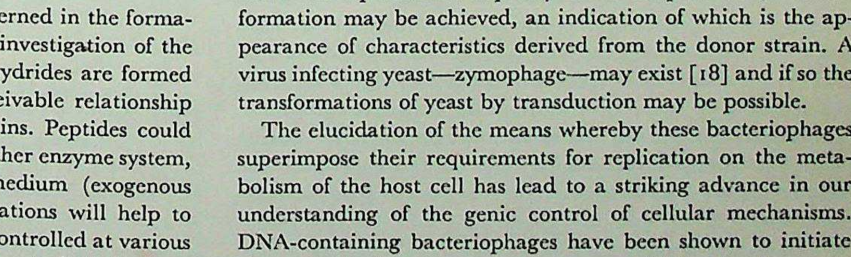
Many current concepts about cellular metabolism have been gained from a study of bacteria. The concluding section considers these studies in relation to the control of cellular metabolism in general, while referring future experiments to yeast where possible.

Cellular mechanism and its future control

Investigations with micro-organisms have yielded much information about the control of cellular functions by the genes. The results obtained are remarkably similar to those obtained with, for example, mammalian cells, even though these show a wide variation amongst themselves because of the diversity of form required to meet their special functions. The study of micro-organisms is particularly convenient because their generally rapid rate of multiplication allows one to observe mutant characteristics that may take many generations to appear. Investigations of this kind can be simplified by selecting the nutrient medium to fit the nutritional requirements of a particular mutant. This technique can also be used to demonstrate the transformation of the hereditable characteristics of a bacterial strain. For example, transformations have been achieved by allowing the DNA of an intact bacterium (recipient) to combine with that isolated from a related strain (donor). By using a medium selective for the donor strain, the recipient acquires the quality, characteristic of the donor, that allows growth in that medium. This admixing of hereditary characteristics may be achieved by the introduction of DNA, isolated chemically from the donor, into the nutrient medium of the recipient strain, with the intention of incorporating the donor DNA into the recipient DNA. A transformation of yeasts using the above techniques has now been claimed [17], and if the claim is valid, it confirms that the DNA of the yeast cell determines its heritable characteristics. In the case of bacteria, an additional means of genetic transfer, called transduction, has been employed. This method involves the transfer of DNA from a particular type of bacteriophage-infected donor strain after cell disruption due to this infection has been provoked; the virus is subsequently liberated and attacks the recipient strain. A segment of the chromosome of the donor is thereby carried into the recipient cell, where it attaches itself to the chromosome of the recipient. If the virus employed does not harm the reproductive capacity of the recipient cell, a transformation may be achieved, an indication of which is the appearance of characteristics derived from the donor strain. A virus infecting yeast—zymophage—may exist [18] and if so the transformations of yeast by transduction may be possible.

The elucidation of the means whereby these bacteriophages superimpose their requirements for replication on the metabolism of the host cell has lead to a striking advance in our understanding of the genic control of cellular mechanisms. DNA-containing bacteriophages have been shown to initiate the synthesis of a new species of messenger RNA after they enter a susceptible bacterial cell. The coding of this new RNA

Figure 4 *A possible role for peptidyl-nucleotidate esters and anhydrides in protein metabolism.*



corresponds to the nucleic acid content of the infecting phage, and so the formation of viral protein proceeds at the direction of the new messenger RNA formed on the nucleic acid of the phage, rather than in accordance with the messenger RNA synthesized on the DNA of the uninfected bacterium. The bacterial cells now make the enzymes required to produce more virus, rather than their normal enzymes, and eventually burst, liberating additional infective virus. Although the more detailed work on this subject has been performed using bacteria, some evidence for a messenger RNA in yeast has been found [19], indicating that the transfer of genetic data via messenger RNA is probably of general occurrence.

A recent publication [20] announced the successful use of a substance having a molecular structure resembling RNA as a substitute for messenger RNA. For example, the addition of polyuridylic acid (a polynucleotide) to the ribosomes extracted from a bacterium, caused the synthesis in this cell-free system of the polypeptide, poly-L-phenylalanine. This product resembles a normal protein, but has only one repeating amino-acid (L-phenylalanine) in its molecular chain instead of about twenty. This exceptionally interesting demonstration of the possible uses of foreign messengers points the way to the control of the enzymic constitution of the cell. Messenger RNA could be isolated from an organism that synthesizes a particular protein and used to direct the formation of that enzyme in another organism, where it might complete a sequence of reactions to give an end-product otherwise unobtainable.

A difficulty to be surmounted in using intact yeast cells is that some of the potential transforming chemicals added to their growth medium are not absorbed into the cell. But this difficulty may not be insuperable. Specific energy-dependent transfer systems exist for the passage of certain materials, such as sugars, through the cell membrane. For example, it is thought that the enzyme (permease) required for the entry of galactose, mediates transfer by the acetylation of this compound [21]. Perhaps other means of overcoming the entry requirements will be discovered.

We must also mention the recent elucidation of the nature of the chemical coding inherent in the structure of the RNA template of the microsomes [22]. It has been suggested that a sequence of three adjacent nucleotides is required to 'recognize' one amino acid prior to its adhesion to the template. This conclusion follows from the discovery that groups of three adjacent nucleotides in the DNA of the gene, and so in the messenger RNA, controlled the enzymic composition of a bacterial cell. Thus each trio of nucleotides in the DNA could be assumed to control indirectly the placing of one amino acid, since the crucial part of the template that forms these enzymes was the messenger RNA formed by the replication of the DNA nucleotide sequence. This feature of the template mechanism has been a controversial matter for some time, and its solution may allow the specific conclusion that three adjacent uridylic acid residues in the template can recognize a phenylalanine molecule. Extensions of this work should solve the coding for the other amino acids, which may be identical for many organisms. Theoretically this knowledge would allow the synthesis of the correct messenger RNA for the production of a particular enzymic protein in an organism, provided the amino acid sequence of the latter had been elucidated. Ability to have such enzymes synthesized to order is surely one of the most desirable goals at present conceivable, for in this way we can directly control the living cell. At the moment, however, the practical difficulties involved in the chemical synthesis of particular ribonucleic acid molecules make the approach very difficult; nevertheless the messenger RNA isolated from one species might be readily used on another.

Acknowledgments

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The spark chamber

D. G. Davis

Spectacular advances have been made in the last few years in the study of unstable sub-nuclear particles. The spark chamber, which shows the path of a charged particle by a series of sparks, is the most recent addition to the instruments that can be used in this field. This article classifies the various types of particle detector, describes the spark chamber, and assesses its value in comparison with the other types of detector that can be used for locating and identifying ionizing radiation.

A whole range of new unstable particles has been produced by experiments, with high-energy protons and neutrons, designed to investigate the forces in the atomic nucleus [1, 2]. These particles can be satisfactorily studied only if suitable detectors are available. An ideal detector would give, at any required instant, the position and identity of the particles that were being examined. A detector, in this sense, means not necessarily a single device but a system that collectively has the required properties. This ideal detector will locate a particle accurately in space and in time.

Particle detectors can be divided into two broad groups, counters and track chambers. A counter is essentially an electronic instrument that produces an electrical signal when a particle enters it, while a track chamber is essentially a visual instrument in which a charged particle produces a track that can be observed by eye or, almost invariably, photographed. The spark chamber is the latest member of the track chamber family. It is in a number of ways closely akin to some types of counter, and, by way of introduction, a brief survey of counters and of track chambers in general will be given. The classification that will be used is shown in figure 1.

The path of a particle in a track chamber can be measured within limits that are very small in comparison with the size of the sensitive region of the chamber. In contrast to this, a counter can indicate only that a particle has entered it somewhere; the spatial limit to the accuracy of location, therefore, is simply equal to the volume of the sensitive part of the counter. The relative values of the two types of instrument are reversed when they are compared in terms of the accuracy of the information they give about the timing of the particles. The particle whose path is recorded in a track-chamber photograph may have entered the chamber at any time during the period that it was sensitive, but the electrical signal from a counter gives the instant at which the particle arrived. The output signal may not occur instantaneously, but it will follow the particle after a fairly definite time-interval, characteristic of the particular counter.

Counters

The accuracy with which the time of arrival of a particle at a counter can be measured is limited by the rate at which the electrical output pulse rises and by any jitter in the start of the pulse. After a counter has produced a pulse, it will not respond properly to a second particle until it has had time to recover from the first. The timing accuracy of a counter, the resolving time, depends to some extent on the circuit that detects the output signal. The recovery time, too, may be determined more by the circuit than by the actual detecting part of the instrument. The remaining characteristics of a counter that are of interest to the experimenter are its size, and its ability to measure the energy of a particle.

Counters depend for their operation on the ionization or radiation produced when a charged particle passes through matter [3]. Ionization of a gas is used in the ionization chamber, the proportional counter, the Geiger counter [4], and in the spark counter. In the first, the ions are simply collected by suitable electrodes with a potential between them, and in the second, the voltage applied between the electrodes is high enough to produce multiplication of the original ions. Both these devices produce outputs that are proportional to the energy loss of the primary particle. In the Geiger counter, the ions multiply until saturation occurs and the size of the output pulse is independent of the nature of the primary particle. The gas pressure in the spark counter [5] is sufficiently high for the ion multiplication to lead to a spark discharge, the nature of which is again independent of that of the source of ionization. There is a solid-state analogue to the ionization chamber in the junction region of p- and n-semiconductor material when a reverse bias voltage is applied.

In the scintillation counter [6], light produced by a charged particle passing through matter is converted to an electronic signal, and amplified by a photomultiplier. The output pulse is proportional to the energy loss of the particle in the scintillating material, which may be gaseous, liquid, or solid.

The Čerenkov counter [7], uses the radiation emitted when a charged particle moves in a transparent material with a velocity greater than that of light in that material. The radiation, which is much weaker than that produced in a scintillating material, is amplified by a photomultiplier to produce a useful signal. The counter can be designed to respond to all particles with a velocity greater than a threshold velocity, or to only those in a narrow range of velocity.

Track chambers

Two of these, the photographic emulsion and the bubble chamber, have already been described in ENDEAVOUR [21, 22]. Track chambers fall into two groups. Those of one group, which includes the photographic emulsion [8] and the diffusion cloud chamber [9], are continuously sensitive. Those of the other, such as the expansion cloud chamber [10] and the bubble chamber [11], have to be triggered and are then sensitive for a short period, after which they need a much longer recovery period before they can be re-triggered. Triggered chambers are of two kinds: the first, of which the expansion cloud chamber is an example, can be successfully triggered after the particle has passed through, while the second, such as the bubble chamber, must be triggered before. This distinction is an important one, since it means that bubble chambers cannot be controlled by a combination of counters detecting particles entering or leaving the chamber, while an expansion cloud chamber can be so controlled. Counter-controlled operation allows the high

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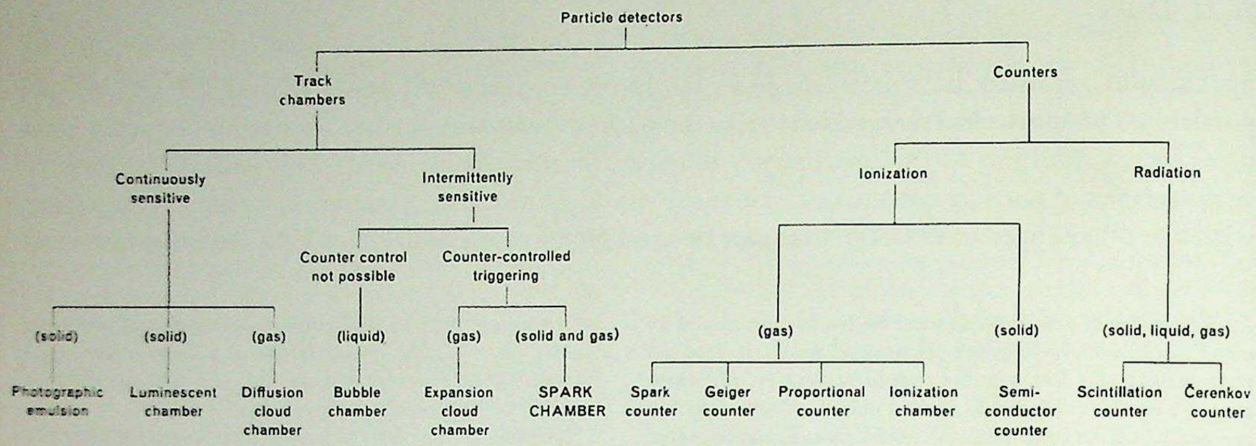
Particle detectors
Track chambers
Counters
Continuously sensitive
Intermittently sensitive
Ionization
Radiation
Counter control not possible
Counter-controlled triggering
(solid)
(solid)
(gas)
(liquid)
(gas)
(solid and gas)
(gas)
(solid)
(solid, liquid, gas)
Photographic emulsion
Luminescent chamber
Diffusion cloud chamber
Bubble chamber
Expansion cloud chamber
SPARK CHAMBER
Spark counter
Geiger counter
Proportional counter
Ionization chamber
Semi-conductor counter
Scintillation counter
Čerenkov counter

Figure 1 *Classification of particle detectors.*

timing accuracy of counters to be used to select an event, involving a number of related particles, that is of interest: the track chamber can then be triggered so that accurate spatial measurements may be made later on the photographs of the tracks of the particles involved in the event.

All track chambers, like counters, depend for their operation on the ionization or optical radiation produced by a charged particle in passing through matter. Uncharged particles can be detected only indirectly, by means of the charged particles they produce.

The photographic emulsion is the simplest form of track chamber. Ionization caused by a fast charged particle moving through a layer of photographic emulsion produces a latent image that, on development, shows the path of the particle as a row of silver grains. The track can then be measured, with a suitable microscope, to a high degree of accuracy. The grains of silver in a track usually have diameters of several tenths of a micron. An emulsion is sensitive from manufacture to development, and it therefore gives no information about the time at which a track was produced. When a particle stops in the emulsion, its energy can be found from the length of the track, and frequently the velocity can be obtained from measurements on other characteristics of the track.

In the luminescent chamber, light produced by a charged particle in passing through a solid crystal of sodium iodide [12] or an array of fibres of plastic scintillator [13] is amplified by image intensifiers and photographed. The sodium iodide crystal or the fibres of plastic scintillator are continuously sensitive, but the image intensifiers are usually operated for only a few microseconds by a pulse derived from a counter control system. The time resolution of the luminescent chamber is thus about a microsecond and the spatial resolution about a millimetre.

Cloud chambers and bubble chambers depend on the phenomena of supersaturation and superheating. A track in a cloud chamber is produced when droplets of liquid condense from a supersaturated vapour on ions produced by a charged particle. The supersaturation may be obtained in two ways: by the rapid expansion of a volume of gas saturated with the vapour, or by the diffusion of vapour from a warm region where it is saturated to a cold one where it is supersaturated. The first method is used in the expansion cloud chamber and the second in the diffusion chamber. The former is sensitive for about ten milliseconds; the latter is continuously sensitive. In counter-controlled operation, the width of a track in an expansion chamber is about a millimetre.

The liquid in a bubble chamber is superheated by reducing the pressure suddenly, after which bubbles of vapour form on the ions produced by a charged particle. The sensitive period of a bubble chamber is about ten milliseconds. It cannot be used for counter-controlled operation, as the lifetime of the bubble-forming centres is rather shorter than the time needed to expand the chamber. On recompression, the bubbles disappear and another expansion may be made after about a second. Measurements can be made on a track to an accuracy of about a tenth of a millimetre. Both bubble chambers and cloud chambers are usually operated in a magnetic field, so that the momentum of the particle can be determined from the curvature of the track. A number of liquids have been used for bubble chambers, of which liquid hydrogen is the most important, since with this liquid any interactions of a particle in the chamber must be with hydrogen nuclei. A particularly beautiful photograph of an antiproton annihilation in a hydrogen bubble chamber is shown in figure 3.

The main features of track chambers and counters are compared in figure 2.

Development of the spark chamber

The spark chamber is a development of the spark counter, which in the simplest form consists of a pair of parallel plates, with a

Detector	Time properties		Space properties	
	Time resolution (sec)	Dead time (sec)	Space resolution (mm)	Typical volume (litres)
Photographic emulsion	—	—	0·001	1
Luminescent chamber	10^{-6}	—	1	1
Diffusion cloud chamber	—	—	0·5	50
Bubble chamber	10^{-3}	1	0·05	500
Expansion cloud chamber	10^{-2}	100–1000	0·5	500
Spark chamber	10^{-6}	10^{-2}	0·5	500
Spark counter	10^{-9}	10^{-2}	100	10
Geiger counter	10^{-6}	10^{-4}	50	1
Semiconductor counter	10^{-8}	10^{-6}	5	0·0001
Scintillation counter	10^{-8}	10^{-6}	100	1
Čerenkov counter	10^{-9}	10^{-7}	100	1

Figure 2 *Typical properties of particle detectors. Some of these properties are subject to wide variation, and these numbers should be regarded as representative only.*

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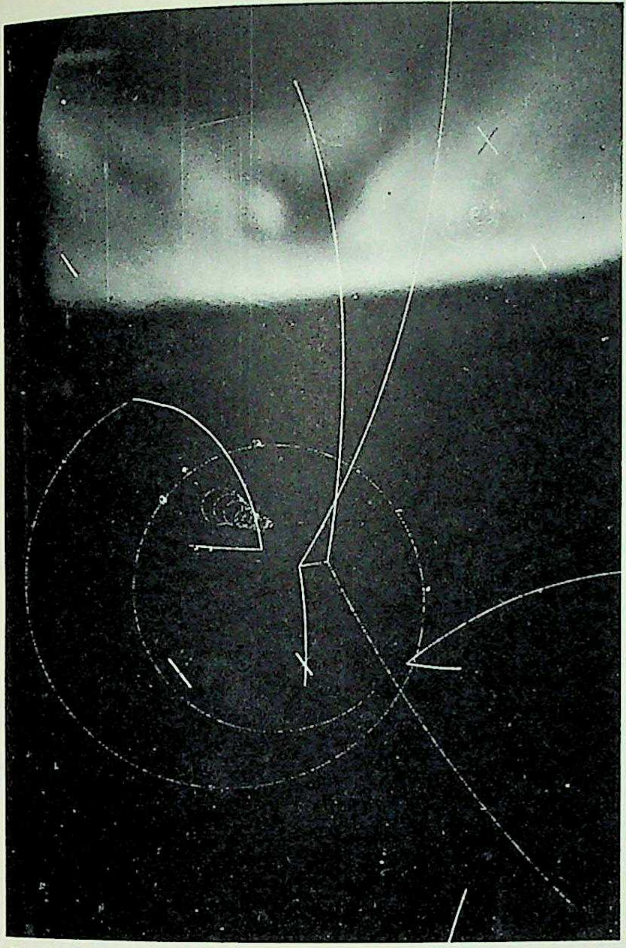


Figure 3 *A bubble-chamber photograph of the annihilation of an antiproton in a French liquid-hydrogen bubble chamber at CERN. The antiproton enters from the top at the right and interacts with a proton to produce four particles, κ°, κ⁻, π⁺, and π°.*

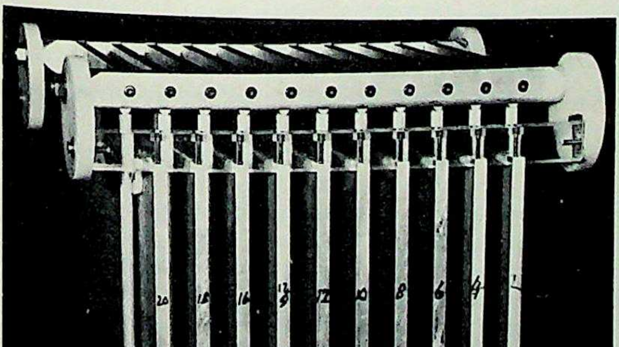


Figure 4 *Thick-plate spark chamber. (Approx. 38 × 38 × 38 cm.)*

high potential between them, in a gas atmosphere [14]. Other forms of spark counter are described by H. Greinacher [15].

In 1955, M. Conversi and A. Gozzini [16] described a new instrument that they called a hodoscope chamber. This is shown in figure 5. It consisted of a number of parallel-plate condensers between the plates of which were packed a large number of thin glass tubes filled with neon at a pressure of about half an atmosphere. When a charged particle passed through the chamber, it was detected by trays of Geiger counters above and below the chamber; a high-voltage pulse was then applied to the condenser plates. A luminous discharge was produced in the tubes the particle had passed through, and this was photographed from one end to give a projected view of the particle path.

Two years later, T. E. Cranshaw and J. F. de Beer published a paper on 'a triggered spark counter' [17]. This was essentially a Conversi hodoscope with the tubes of neon replaced by air at atmospheric pressure, and the plate separation reduced to a millimetre. A series of sparks, that could be photographed, was produced between the plates along the path of the particle.

The essential step in producing a practical chamber for high-energy particle research was taken by S. Fukui and S. Miyamoto [18] when they used a mixture of neon and argon at atmospheric pressure instead of air. This gave two major improvements over the chamber of Cranshaw and de Beer. It was possible to obtain sparks for a group of particles all going through the chamber at the same time, and the use of noble gases gave a much more rapid recovery.

It was shown by G. R. Burleson, A. Roberts, and T. A. Romanowski [19] that it is quite practicable to use a parallel-plate spark chamber in a magnetic field of 13 000 gauss. The sparks showed that the particles causing them moved in curved paths. This made it possible to determine their momentum and the sign of their charge.

Construction and operational characteristics

The construction of a spark chamber depends considerably on the purpose for which it is intended. The trajectory of a particle is shown most accurately when the plates of the chamber are made as thin as possible. A chamber can be made of thin aluminium plates mounted in 'shelves' in a cemented Perspex box, through which gas flows continuously. This method of construction can be used only when the gas pressure is equal to

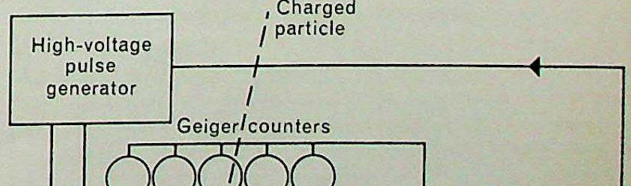


Figure 5 *Hodoscope chamber of Conversi and Gozzini.*

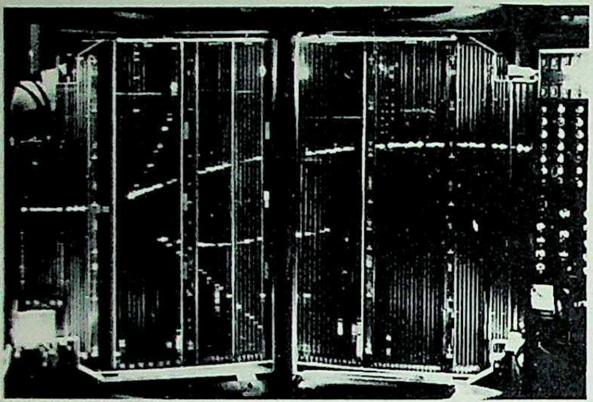


Figure 6 *Photograph taken with a spark chamber in a magnetic field. A π-meson enters on the left hand side, it collides with a proton producing two neutral particles, which cannot be seen in the spark chamber, each of which decays into a pair of oppositely charged particles. (Photograph reproduced by courtesy of the Argonne National Laboratory group at CERN.)*

atmospheric pressure. A chamber of thick aluminium plates is shown in figure 4. It is housed in a massive box that can be completely evacuated and then filled with gas. Helium, argon, neon, and mixtures of these gases have been used in spark chambers. Neon with a small proportion of argon is a very suitable gas.

The counter control system of a spark chamber is shown in figure 7. In this example it is required to trigger the spark chamber when a particle passes through counters A and B and fails to reach counter C. Events are thus selected in which the particle is stopped or scattered in the plates of the chamber. The high-voltage pulse is produced by connecting a condenser, which has previously been charged to the high voltage, to the plates of the chamber through an electronic switch. The switch is either a spark gap or a hydrogen thyratron, triggered by the output from the counter control system.

The sparks in a chamber are normally photographed from two mutually perpendicular directions in order to locate them in three dimensions. It is convenient to combine the two views on one photograph by means of mirrors as shown in figure 7. So that the camera can see the full depth of the gap between the plates a field lens, which also destroys the perspective, is used. This lens can either be cylindrical, with its axis parallel to the plates, or a normal spherical lens.

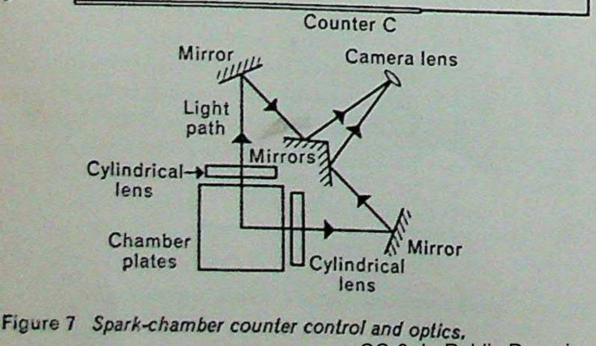
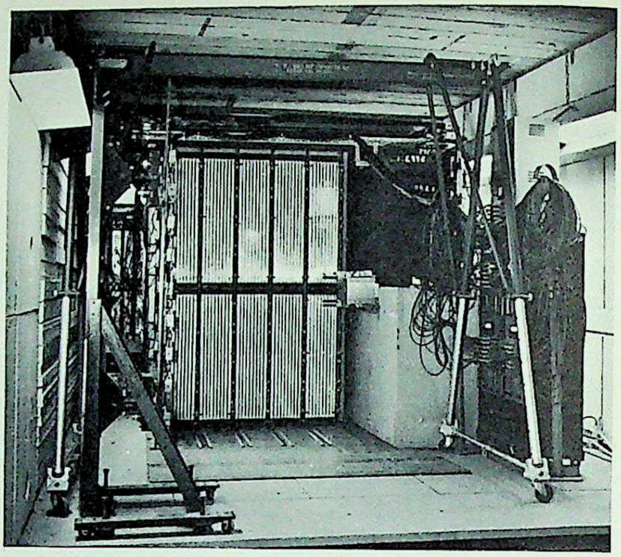


Figure 7 *Spark-chamber counter control and optics.*



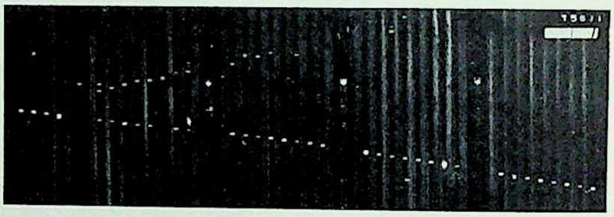


Figure 8 (top) *Columbia University spark chamber installed at the Brookhaven Alternating Gradient Synchrotron for the neutrino experiment. (Photograph by courtesy of Brookhaven National Laboratory.)*

Figure 9 (bottom) *Photograph of a neutrino collision in the Columbia University spark chamber. The spark tracks show a long straight track of a μ-meson produced by the incident neutrino. Only μ-mesons were produced by the neutrinos in this experiment; equal numbers of μ-mesons and electrons would occur if there were only one type of neutrino. (Photograph by courtesy of Professor L. M. Lederman.)*

There are three time-intervals that are of importance for a spark chamber. The first of these is the sensitive time, the time after the passage of an ionizing particle during which a spark will be produced if the high voltage is applied; it is of the order of one microsecond. The second is the breakdown time, the interval between the application of the high voltage and the appearance of the spark. This depends on the rate of rise of the high-voltage pulse and is about 2×10^{-8} sec. The third is the recovery time, the period that must elapse after a spark before the high voltage can be re-applied without causing the previous spark to re-ignite.

A clearing field of a few hundred volts per centimetre is usually applied between the plates of a chamber to sweep away the electrons produced in the gas. This reduces both the sensitive time and the recovery time. The sensitive time can be varied between 0·3 μsec and 10 μsec by varying the clearing field. The rate at which a spark chamber can be triggered is usually limited in practice by the speed with which the film in the camera can be wound on or by the time required to recharge the reservoir condenser, rather than by the recovery time itself.

The accuracy with which the path of a particle can be determined from the sparks depends to some extent on the separation of the plates. Gaps of 2 to 10 mm have been used. In narrow-gap spark chambers, for particles moving perpendicular to the plates, the sparks are distributed about the particle path with a root-mean-square deviation of about 0·3 mm. When the particle path is inclined to the plates the accuracy is less and, at angles greater than 45°, multiple sparks may be produced.

Applications

The main use of the spark chamber is to study the production, interaction, and decay of the elementary particles. Up to the present these processes have been examined with nuclear emulsions and bubble chambers, and the less complicated phenomena measured with greater accuracy with systems of scintillation and Čerenkov counters. The difficulty with bubble chambers is that each individual event has to be scanned by a human operator, to see if it is of the right type, and then measured, and the results processed on an electronic computer. There is thus an economic limit to the number of events that can be studied, and hence to the statistical accuracy of the results. It is possible to select much larger numbers of events with counters, but this method is impracticable for events involving many particles. The simplicity and relative cheapness of the spark chamber make it possible to build a chamber specifically for a single experiment. This is not economically feasible for a large bubble chamber, which is so expensive that it must be a compromise design suitable for a number of experiments. Large spark chambers can be built in a few months, while a large bubble chamber may well take several years. In an experiment using spark chambers the cost of the chambers themselves will be quite a small fraction of the total cost of the experiment.

The chief advantage of the spark chamber over the bubble chamber is that it can be used where the number of particles passing through the chamber is very high, say 10^6 per second, and comparatively rare events produced by them can be selected and recorded. The spatial resolution of the bubble chamber is an order of magnitude better than that of a spark chamber, but as its sensitive period is some ten thousand times longer, it can be used only with much smaller fluxes of particles passing into the chamber. Bubble chambers are normally used at expansion rates of one every few seconds. This is very suitable for accelerators, such as the CERN proton synchrotron at Geneva, that produce one pulse of particles every few seconds. The bubble chamber is much less suitable for high-intensity machines, such as the Princeton-Pennsylvania proton synchrotron, which will produce output pulses at a rate of twenty a second.

Highly elaborate methods have to be used to separate physically the various types of particle that occur in the secondary beams from the large accelerators. This is essential for bubble-chamber experiments on these beams, but it is unnecessary for spark chambers, provided that the different particles can be identified by a counter selection system.

Spark-chamber photographs contain less information than bubble-chamber photographs and should therefore be less difficult to analyse automatically. One of the major difficulties in bubble-chamber physics is the enormous labour of analysing the photographs produced, and it is to be hoped that this will, in the long run, prove to be less serious with spark-chamber photographs. It may prove possible to feed spark-chamber data directly into a computer, thus avoiding the photographic stage.

Many experiments using spark chambers are now in progress or preparation, but very few have yet been published. Figure 6 shows a spark-chamber photograph taken in a magnetic field by the Argonne group during an experiment at CERN. In all, over 400 000 photographs were taken. The gap in the tracks in the middle of the chamber is apparent rather than real. It is produced by the rather elaborate optical system needed to photograph the part of the chamber otherwise hidden by the magnet.

The most important experiment so far completed using a spark chamber is the one, carried out at the Brookhaven National Laboratory in the United States, that established the existence of two types of neutrino [20]. The spark chamber was used to detect the μ-mesons produced when a neutrino interacts with a neutron or an anti-neutrino with a proton. The chief requirement was to provide as much matter as possible in which the neutrino could interact. The detector (figure 8) consisted of an array of ten units, each weighing a ton, containing nine aluminium plates 112 cm by 112 cm by 2·54 cm thick, separated by 0·95 cm gaps. Scintillation counters were placed between the units of the spark chamber, and the whole was surrounded by anti-coincidence counters. The counter control was arranged to pulse the spark chamber when a particle appeared inside it without any charged particle going through the anti-coincidence counters. Figure 9 shows a neutrino collision. An electrical signal from the proton synchrotron producing the neutrinos suppressed any triggering that did not occur in exact synchronism with the bursts of neutrinos. The discovery made in this experiment would not have been possible without the invention of the spark chamber.

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The origins of the metric system

Douglas McKie

Britain is, at present, considering the adoption of the metric system of weights and measures. When this system was first introduced, in France after the Revolution, the intention was that it should be based on a natural standard, common to all men, in accordance with the aims of the Revolution. This article describes the antecedents of the system, the way in which the unification was first attempted, and how it was linked with the decimal system.

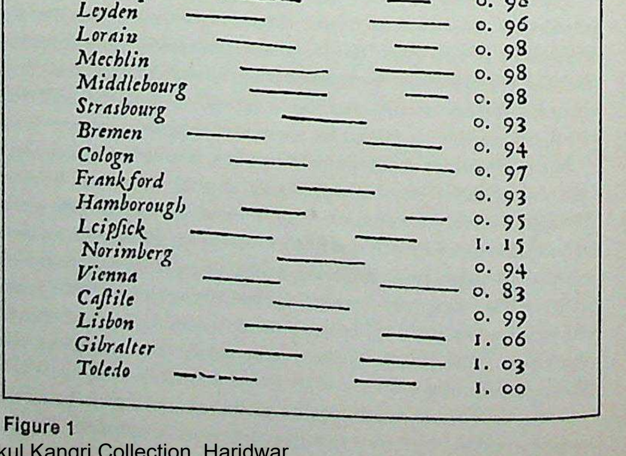
The first effective step towards the formulation and establishment of a national system of weights and measures in decimal notation was taken in France within a year of the outbreak of the Revolution in 1789. For many centuries the Kings of France and their Ministers had striven in vain against the use of a bewildering variety of weights and measures. They wished to effect a reform that they considered necessary for their fiscal administration and in the interests of commerce, but they had failed for two reasons. One was the general and ingrained opposition to change, the other, the resistance of the seigneurs, petty rulers in their provinces, to proposals that would prevent them from using two standards with, of course, increased profit to themselves. Units varied from province to province and even from town to town; they varied greatly even within the same province. In Maine-et-Loire there were 110 different measures for corn; in Ardèche there were 10 different units of weight; and in Nord there were 21 varieties of the pound weight. In eighteenth-century France, with the largest population in Europe, and engaged mainly in agriculture and domestic industry, the situation was chaotic.

As for Europe in general, the state of affairs was not much better. John Harris published his *Lexicon Technicum* in London in 1704; it was the first technical dictionary to be compiled [1]. He gave a table (figure 1) of the relative weights of the pound avoirdupois used in various cities of Europe, and in Cairo and Constantinople, compared with the English pound. He included another table, far too large to be shown here, for the 100-pound weight of Antwerp compared with that of other cities and towns in different parts of the world, ranging from Abbeville to Aleppo, from Amsterdam and Calais to Alexandria and Calicut and other centres of international trade. A further long table (partly shown in figure 2) related the English foot to its corresponding foreign measure. It is interesting to note that there is in this table an extra column in which the proportions are expressed in English in a decimal notation using inches, an early use of that system in English books. Harris had, in fact, included in his *Lexicon* an article on decimal fractions, describing the arithmetical processes of addition, subtraction, multiplication, and division in this notation.

The decimal system was first described in detail towards the end of the sixteenth century by Simon Stevin of Bruges (1548–1620) in his *De Thiende* (Leyden, 1585). This was translated into French by the author as *La Disme* (Leyden, 1585) and into English by Robert Norton as *Disme: The Art of Tenths, or, Decimall Arithmetike* (London, 1608). (The word *disme*, 'tenth' or 'tithe', survives in the American 'dime' or tenth of a dollar.) Stevin's book brought decimals into the structure of arithmetic, but his notation was unwieldy, and the decimal system did not come into general use until more than two centuries later.

In the years immediately preceding the Revolution, one of the members of the Royal Academy of Sciences most interested in the use of the decimal system was Antoine-Laurent Lavoisier (1743–94). He had used it as an alternative to the older system for the expression of subdivisions of weights in his classic memoir on heat, written in collaboration with Laplace and published in 1784. In his *Traité élémentaire de chimie* (Paris, 1789), he used it more generally and gave tables for the conversion of divisions and subdivisions of the pound weight and the inch into decimal notation. He was a powerful advocate of the decimal system.

Among the Academicians, suggestions had been made from time to time about the basing of a new and standard system of weights and measures on some suitable physical constant. Jean Picard (1620–82), the astronomer, suggested in 1671 the length of the seconds-pendulum as a standard, although he seems to have suspected that this length varied with latitude. This was demonstrated a few years later by the observations made in Cayenne by some of his colleagues. Another astronomer, Jacques Cassini (1677–1756), proposed in 1720 that one-hundredth part of an arc of one second of the meridian should be taken as the standard foot. However, the Academy considered that the accurate measurement of the meridian would be difficult. There was already disagreement about such results as had been obtained, and more was to follow. In 1748, the mathematician Charles-Marie de la Condamine (1701–74) recommended the length of the seconds-pendulum at the Equator as a standard. The Academicians were slowly



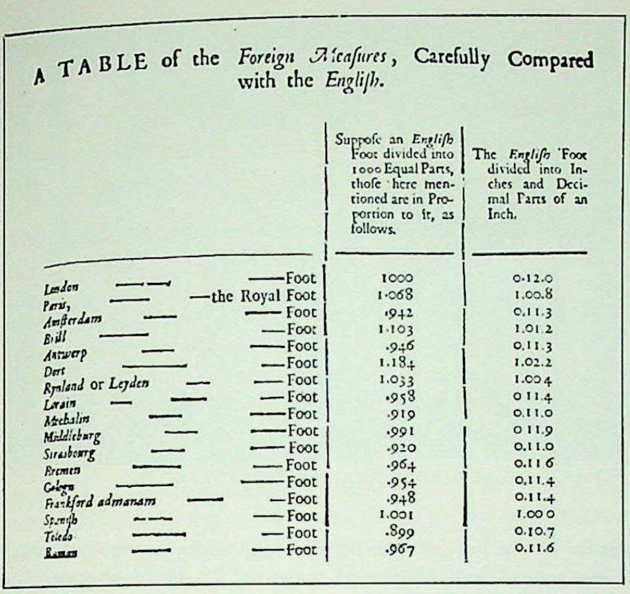
A Table of the Foreign Pound Averdupois, *compared with our Pound* Engliſh.

	The Pound *Averdupois* into 100 Parts.
London	100
Paris	0. 93
Lyon	1. 09
Bologn	0. 89
Amſterdam	0. 93
Antwerp	0. 98
Leyden	0. 96
Lorain	0. 98
Mechlin	0. 98
Middlebourg	0. 98
Strasbourg	0. 93
Bremen	0. 94
Cologn	0. 97
Frankford	0. 93
Hamborough	0. 95
Leipſick	1. 15
Norimberg	0. 94
Vienna	0. 83
Caſtile	0. 99
Lisbon	1. 06
Gibralter	1. 03
Toledo	1. 00

Figure 1

Douglas McKie, *Ph.D., D.Sc., F.R.I.C., F.R.S.E.*

Was born in 1896. He entered University College, London, in 1920 and graduated in chemistry, and is now Professor of the History and Philosophy of Science in the University of London. He has written extensively on the history of chemistry.



A TABLE of the *Foreign Meaſures*, Carefully Compared with the *Engliſh*.

	Suppoſe an *Engliſh* Foot divided into 1000 Equal Parts, thoſe here mentioned are in Proportion to it, as follows.	The *Engliſh* Foot divided into Inches and Decimal Parts of an Inch.
London ——Foot	1000	0.12.0
Paris, —the Royal Foot	1.068	1.00.8
Amſterdam ——Foot	.942	0.11.3
Brill —Foot	1.103	1.01.2
Antwerp ——Foot	.946	0.11.3
Dort —Foot	1.184	1.02.2
Rynland or *Leyden* —Foot	1.033	1.004
Lorain —Foot	.958	0 11.4
Mechalin ——Foot	.919	0.11.0
Middleburg ——Foot	.991	0 11.9
Strasbourg ——Foot	.920	0.11.0
Bremen —Foot	.964	0.11 6
Cologn ——Foot	.954	0.11.4
Frankford admanam —Foot	.948	0.11.4
Spaniſh —Foot	1.001	1.00 0
Toledo —Foot	.899	0.10.7
Roman ——Foot	.967	0.11.6

Figure 2

moving towards a solution of the problem, but in doubt and difficulty. They had long been concerned in the measurement of an arc of the meridian on account of their very active interest in the greater problem of the figure of the Earth – whether it was flattened or elongated towards the poles. They had organized a number of expeditions for this purpose, including two memorable ones, to Peru and to the Arctic Circle; and they had made this problem almost their own.

Meanwhile, public dissatisfaction was growing. The States-General was summoned to meet in 1789 for the first time since 1614. A demand for a national system of weights and measures was included in the *cahiers de doléances*, the writs of grievances submitted by the Provincial Assemblies and other elective bodies to the States-General. While there was nothing new in this, since it had been made in the *cahiers* submitted in 1576, the time was ripe for reform. The monarchy still existed in 1789–90, and the National Assembly provided a strong central government in Paris confident of its ability to impose its will on provincial governors and officials. The assembled representatives of France wanted a national system of weights and measures; two recent Ministers, Turgot and Necker, had approved of it; and the Academy of Sciences was in favour of the change as increasingly necessary because of the advances in the exact sciences of mechanics, astronomy, physics, and chemistry, and also because of the outstanding French achievements in cartography.

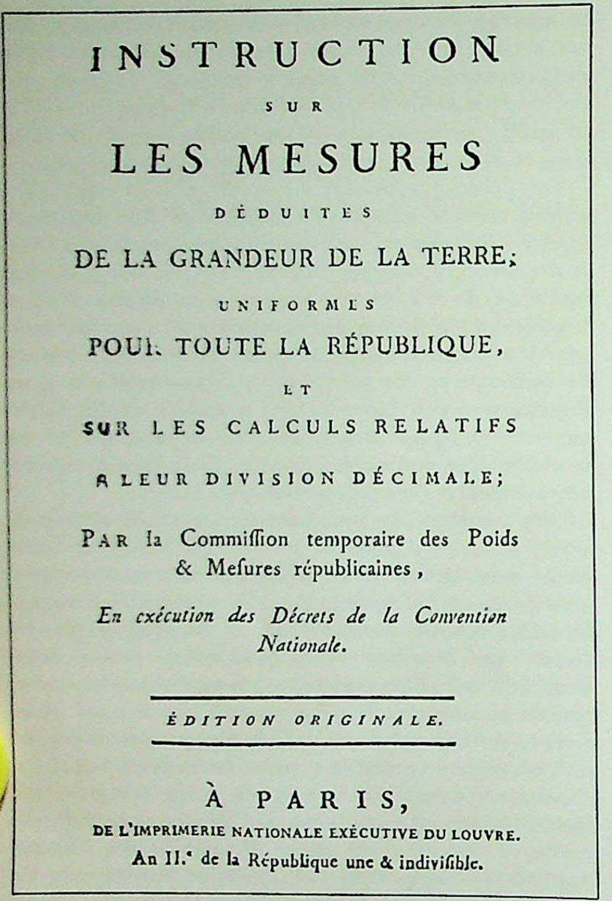
On 8th May 1790 the National Assembly decreed that the Academy should formulate a new system of weights and measures based on a suitable physical constant, the length of the seconds-pendulum, so that the new units could be adopted by all nations. It was to be a universal rather than merely a national system. There was no mention of decimal notation. The Academy was to be responsible for preparing models of the new standards, which were to be despatched to all cities and towns in France; six months after the despatch of the models the new system was to replace the old measures. The new rulers of France underestimated the labour involved.

In the Academy, matters went differently. While the Academicians were already convinced that the unit of length should be based on some physical constant, they were scientists as well as Frenchmen. Although the length of the seconds-pendulum under stated conditions would have been a suitable constant, they decided to measure also an arc of the meridian because they were not satisfied with previous attempts at this, and because the result might resolve some differences within their company about the shape of the Earth. Moreover, the decree of the Assembly provided them with money that could be used in the investigation of this leading scientific problem. As Biot wrote some years later, science also has its politics.

The Academy appointed a commission of its most distinguished members to report on the problem. The commission consisted of Condorcet, Lavoisier, Lagrange, Borda, and Tillet. It recommended, on 27th October 1790, the use of decimal notation in the new system, and a second commission, to which Laplace and Monge were added, recommended on 19th March 1791 that the measurement of an arc of the meridian would be preferable to the use of the seconds-pendulum. From that measurement, the length of a quarter of the Earth's meridian would be derived and one ten-millionth of this would be taken as the unit of length. The National Assembly adopted these recommendations on 26th March.

Only the Academy appreciated the magnitude of the task, which was to be delayed for years by the decision in favour of the measurement of the meridian. It divided the work among a number of commissions. Among these, Méchain and Delambre were to measure an arc of the meridian between Dunkirk and Barcelona; Borda and Coulomb were to determine the length of the seconds-pendulum (retained for obvious reasons *vis-à-vis* the Assembly); and Lavoisier and Haüy were to determine the weight of water corresponding to the unit of volume on the new scale. Instruments had to be constructed, names had to be given to the new units and their multiples and subdivisions, and the new units had to be compared with the old ones. Meanwhile, the National Assembly was replaced by the Legislative Assembly and the latter by the National Convention, and all these bodies regarded the matter as urgent. However, it was not until 1st August 1793 that the Convention was able to make a further decree about the new system. Since the work was largely incomplete, the decree was based on an earlier measurement of the meridian by Nicolas-Louis de Lacaille (1713–62), who had determined that at 45° latitude a degree of the meridian measured 57 027 *toises* (a *toise* was 6 Paris feet). Decimal notation was prescribed and names were given to the new units. Among these was the *mètre*, but not yet the *gramme*, which was named at this time the *gravet;* the unit of weight chosen was the weight of unit volume of distilled water weighed *in vacuo* at the temperature of melting ice. Standards were to be prepared under the supervision of the Academy and sent to all local administrations throughout France, and the Academy was to prepare a book on the new system with full information about the measures, expressed in decimal notation, for all citizens. These changes were to be incorporated in the textbooks of arithmetic used in the schools, and the new system was to become obligatory on 1st July 1794. The text of the decree was published in Rozier's *Observations sur la physique* [2] in September 1793.

Political events now took a new turn. On 8th August 1793, a week after the new decree, the Academy of Sciences and all other learned societies were suppressed by order of the Convention. A year earlier France had become a republic and the book that the Academy was to prepare appeared under the aegis of a new body, the *Commission temporaire des Poids & Mesures républicaines*. For the title-page of this rare work see figure 3. It is an octavo volume of about 260 pages with many tables, but it is mainly a simple treatise on decimal arithmetic as applied to the new measures. The name of Lacaille, on whose work the fundamental unit of the system



INSTRUCTION

SUR

LES MESURES

DÉDUITES

DE LA GRANDEUR DE LA TERRE;

UNIFORMES

POUR TOUTE LA RÉPUBLIQUE,

ET

SUR LES CALCULS RELATIFS

A LEUR DIVISION DÉCIMALE;

PAR la Commiſſion temporaire des Poids
& Meſures républicaines,

*En exécution des Décrets de la Convention
Nationale.*

ÉDITION ORIGINALE.

À PARIS,
DE L'IMPRIMERIE NATIONALE EXÉCUTIVE DU LOUVRE.
An II.ᵉ de la République une & indiviſible.

Figure 3

was based, did not appear in its pages, perhaps because he had been a member of the Academy and a priest. His value of 57 027 *toises* was smuggled into one of the arithmetical exercises given as examples of decimal arithmetic.

Delay succeeded delay in the completion of the original programme. Lavoisier was arrested as a former Farmer-General on 28th November 1793 and executed on 8th May 1794. He had fought to the last against the suppression of the Academy, especially in the interests of the work on the new weights and measures. As Treasurer of the Academy he had had great difficulty in obtaining the money voted by the Assembly for the work and for the necessary instruments and apparatus. Thus in 1792, when some of the instruments for Méchain and Delambre were ready, they had had to begin their work while the grant for that year was still unpaid. During the winter of 1792, Lavoisier had worked with Haüy on the determination of the density of water. He used the balance constructed for him by Fortin. This historic instrument is now at last preserved in Paris (figure 4). Although he had been the effective organizer of the work of the Commission of Weights and Measures, he was, with Laplace, Delambre, Brisson, and Borda, dismissed by the Committee of Public Safety on 23rd December 1793 (a month after his arrest) on the grounds that the Republic could entrust duties only to men on whose republican virtues and hatred of kings they could confidently rely. Prieur, deputy for La Marne in the Convention, was put in charge, and he made it an administrative bureau rather than an institute of scientific research. But some interesting changes were made in the names of the new

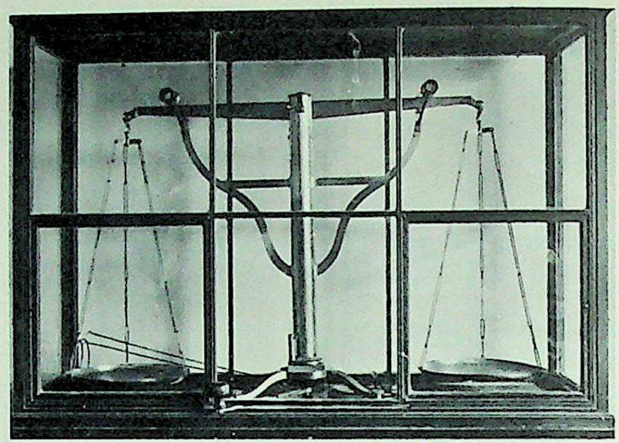


Figure 4 *Lavoisier's balance, constructed by Fortin.*

units in a report of 7th April 1795, when the now familiar *litre*, *gramme*, and *kilogramme* appeared for the first time. The work was thus effectively interrupted until the *Institut National* was established on 25th October 1795 as successor to the suppressed *Académie des Sciences;* it was completed late in 1798 and finally described in three large quarto volumes entitled *Base du système métrique décimal* (Paris, 1806–10). In the course of the measurements it was found that the Earth was not a perfect spheroid of revolution. One meridian differed from another in length, and while the Earth was an oblate spheroid in its general shape, there were differences in the length of a degree of arc along any one meridian; occasionally, the small systematic change consequent on the general flattening towards the Poles was reversed. Thus the fundamental unit of length was ultimately arbitrary and the doctrinaire egalitarianism that had once inspired the Revolutionary reformers to measure the meridian common to all men and to base upon it a universal system of weights and measures had to be quietly forgotten. Further, the metallic bar used as the standard metre was standard at 0°C, while the unit volume of distilled water was measured, not at 0°C as originally decided, but at 4°C (the temperature of its maximum density) and the unit of weight was therefore not directly related to the unit of length. However, the completion of the task remains one of the great achievements of French science, and it was carried through to its final success in the face of discouraging difficulties and disheartening political conditions and interference – and often amidst the distractions of war.

The revised standards of length and weight were ready on 22nd June and approved as legal on 10th December 1799, becoming compulsory in 1801; but in practice they were accepted slowly, and as late as 1837 the French Government had to pass a law forbidding under severe penalties the use of the old measures as from 1st January 1840. Many countries have adopted the system; in Great Britain its use has been permitted since 1897.

Finally, we may note that one of the objects of the French reform, the use of an invariable universal natural standard, has at last been achieved. The wavelength of a line in the spectrum of krypton-86 has recently been adopted as the basis of the international unit of length.

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The sense of direction in migratory birds

W. Delvingt and J. Leclercq

It has been found that migratory birds follow a direction that is innately determined, and that they can correct deviations caused by weather or topography. Some birds, in addition, can find their way home when released in unknown territory. This article discusses the mechanisms that have been suggested for this orientation and navigation, and describes experiments to test the theories.

Bird migration has always aroused the curiosity and imagination of man, although it was not always recognized as migration. The theories formerly put forward to explain the periodical disappearance of certain birds were sometimes highly original [1], and it was not until the end of the nineteenth century that sufficient observations had been made to allow an approach to a scientific study of migration. The first half of the twentieth century saw the introduction and the rapid expansion of ringing operations in Europe and the United States, and the development of physiological research. Complete reviews of the advances made have been published [1, 2, 3, 4]; our intention here is to review the methods and conclusions concerning the direction-finding sense in migratory birds.

Methods

Ringing

Ringing organizations throughout the world have collected and collated a lot of information, and one might think that it is simple to answer the main queries about migration routes and the methods of specific migrations. All that seems to be needed is to plot the data on a map, analyse them statistically, and find out which facts do not vary and which occasionally do. However, it would take hundreds of years of close observation for systematic ringing to answer all the questions, even though this method has the great advantage of being able to give exact information of place of departure and of arrival, and of the effect of weather conditions.

However, the proportion of ringed birds that are caught again remains very low—almost nil in certain areas and for certain species. In most cases, the maps showing the results give only a vague idea of the actual routes, and a study of local weather bulletins does not clearly explain the observations.

The method relies much on hazard, and it rarely reveals more than the broad outlines of the behaviour of species. Irreplaceable as it is as a biogeographical method, it becomes laboured and insignificant when it comes to understanding the methods, ecological relations, and determinism of migrations. It is therefore necessary to resort to experiment and the testing of hypotheses.

Direct observation

It is important to realize that all migrations are orientated; this is why their direction has often been associated with meteorological phenomena and topographical peculiarities. Many migration routes follow the coasts or large valleys, avoiding chains of high mountains and large sea areas. Thus, European populations of white storks (*Ciconia ciconia*) use two different routes to Africa, one through the straits of Gibraltar, the other through the Bosphorus. Both avoid crossing the Mediterranean. Many migrations, though, are known that brave the open sea; even among the storks, some individuals venture successfully over it.

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The direct observation of migratory voyages has shown that many birds modify the direction of their flight when the wind or the landscape changes. These observations have been supplemented by the use of radar, and by watching the flight of nocturnal migrants across the disk of the moon. It has been possible to show, in some cases, that the direction is related to that of the prevailing winds, which suggests a dependence on air temperatures.

This might explain the two different routes followed by the red-backed shrike *Lanius collurio* studied by R. Verheyen [5]. It is particularly sensitive to cold nights, and it appears to migrate to Africa on a cold leading wind and to return to Europe on a warm one. The date of its arrival in May in Europe seems to coincide with that of streams of hot air from the south-east (figure 1). The meteorological or geographical facts do not, however, justify the supposition that migrations are little more than the mere drifting of birds on air currents. Migrations are actively orientated, and we can in fact state that there is a general itinerary with a definite orientation. Changes of direction are not imposed on the bird by weather or topography; they are its response to them.

Navigation

Most birds have an excellent visual memory and their sight is extremely acute. That is why these characteristics have often been thought to be used by the migrants for orientation and navigation.

It is well known that racing pigeons have to be trained to exercise their memory of their surroundings before being able to make long-distance return flights. They lose their way easily when visibility is bad or when the countryside is under snow. They are unable to return, even a short distance, when blinded. Their visual memory is extraordinarily faithful. Thus B. F. Skinner [6] trained four pigeons to peck in certain places on an aerial photograph. Four years later, the birds pecked the learned positions.

Of course, acuteness of sense and visual memory are not alone sufficient to explain the performance of migratory species. In the first place, various experiments show that some migrants travel along an innately determined direction. Thus, W. Rüppell [7] captured 896 hooded crows (*Corvus cornix*) at Rossitten during spring migration, when these birds usually migrate to the north-east. He let them loose at Flensburg, quite outside their normal territory. The crows flew off parallel to their usual direction towards the north-east (figure 2). In the same way, E. Schüz [3] and A. C. Perdeck [8] showed that young starlings, captured during their autumn migration and

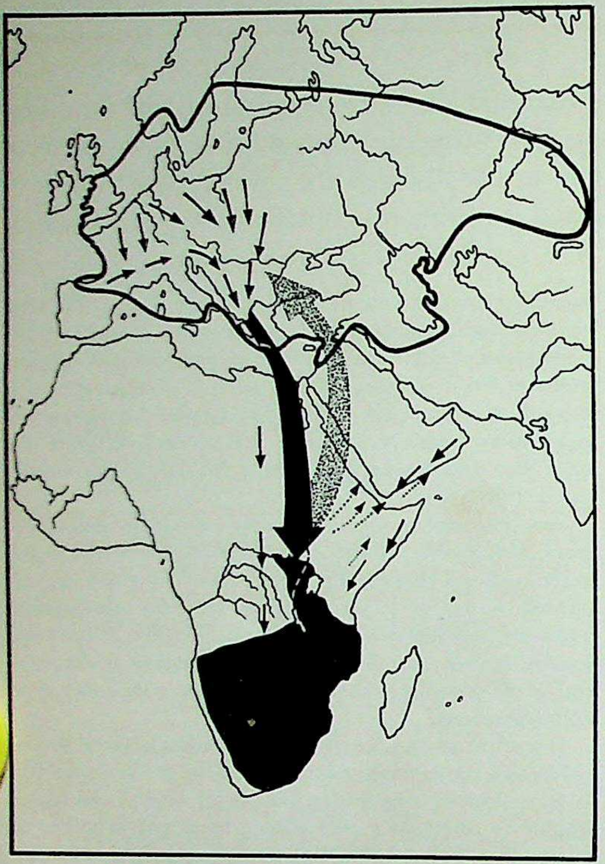

Figure 1 *Migration of the red-backed shrike* Lanius collurio *(Verheyen, 1951).*

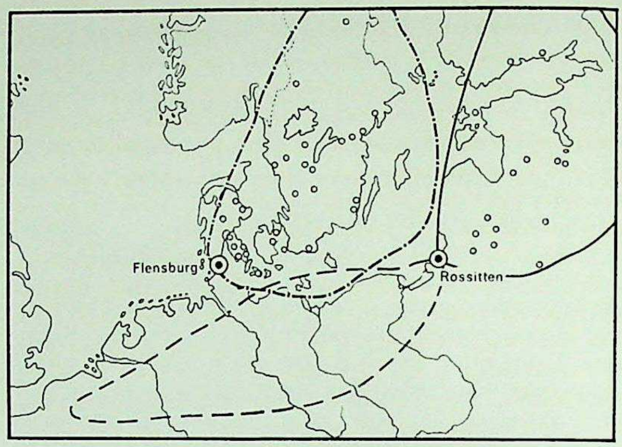

Figure 2 *Rüppell's experiment. Normal breeding area in continuous line. Normal winter quarters in broken line. Displaced breeding ground in broken line with dots. (After Rüppell, 1944.)*

moved away from their normal route, maintained the original direction.

In addition to this, some migrants seem capable of real navigation—that is, they can fly a course which will bring them to their goal from wherever they happen to be. The goal may be determined without previous experience, as when young migrant birds find their own way to their winter quarters, or by learning, as in homing experiments.

Many workers have captured birds in the nest and released them later, sometimes a considerable distance away. The percentage of returns varies greatly according to the species, even in the case of very closely related ones. For those which are clearly migratory, it is generally significantly above that statistically to be expected if flights were made at random.

Some migratory birds have also been captured on their way to their winter quarters, and then released outside their normal migration route. We have already seen that young starlings, if displaced, maintained their normal migration direction. Adult starlings, on the other hand, changed direction in order to reach their previous winter location [8]. The precise interpretation of these experimental results has, however, been criticized [9], as some erratic birds with no fixed winter quarters in natural conditions, when captured in their winter location and released a considerable distance away, return to it.

The interpretation of homing experiments is also rendered difficult by the occurrence of 'nonsense orientation'—that is, a statistically significant orientation of the released birds in a direction which bears no known relation to their home. In other cases a preferential orientation varying with the geographic location of the home but not related to its direction from the particular release point has been found [10]. Such phenomena have been studied in the starling *Sturnus vulgaris* [11], the common tern *Sterna hirundo* [12], and the duck *Anas platyrhynchos* [13, 14] and remain unexplained.

Some displacements occur naturally: certain migrants when blown off course orientate themselves towards their winter quarters. This fact has been frequently noticed, but authors differ considerably when it comes to assessing its relative importance. It seems, however, that young birds are more widely affected than adult individuals. Therefore, H. C. Wallraff's assertion [15] that the direction to be taken is in many cases innate, while the geographical location of a goal area must be learned or imprinted through experience, based mostly on Perdeck's results [8], has yet to be proved.

The sensorial mechanisms of orientation

Early theories

What is meant by 'sense of direction'? The word 'sense' supposes the use of a sensory organ and of a mechanism of perception that can be tested experimentally. It has been supposed that birds can determine the co-ordinates of a particular place and make their way towards those of their territory, and a number of ways of doing this have been suggested. Some undoubtedly ingenious ideas have been left unexplored because they could not be tried experimentally.

In 1946, G. Ising [16] suggested that the sense of direction in birds might be explained by their perception of mechanical forces resulting from the rotation of the Earth. He made a precise study of the forces to which a moving object is submitted that might play a part. He imagined that birds perceive the variations of these forces through the semicircular canals in the ear. Although firmly founded on physical considerations, this theory has been abandoned because it postulates an improbably delicate sensorial mechanism. The hearing of birds is less sharp than that of mammals; nothing in the structure of their ears suggests a sufficiently high sensitivity for such variations to be detected; even mammalian ears cannot detect such minute changes among those caused by other agents, such as turbulence.

An older theory suggested that birds were able to detect the electromagnetic forces of the Earth's field. In 1947, A. J. Yeagley [17] proposed a combination of this theory and that of Ising's outlined above. He supposed that birds determine their latitude from the Coriolis force, which arises from the effect of the Earth's rotation on a moving object, and their longitude from the variations in intensity of the vertical component of the Earth's magnetic field.

The Coriolis force is known to be responsible for deviations in the paths of shells, rockets, and air masses. It is nil at the Equator, and at its maximum at the poles. The lines of equal intensity are, of course, the parallels of latitude. The lines of equal intensity of the vertical components of the Earth's magnetic field, on the other hand, form closed curves about the magnetic poles. It is thus conceivable that this double system of reference allows the bird to find its bearings.

Yeagley located two different places in the United States with identical values of the two forces (figure 3). One, in Pennsylvania, was chosen for the breeding and training of pigeons. The other was in Nebraska; Yeagley built a pigeon-house there that was similar to that with which the Pennsylvania pigeons were familiar. Some pigeons were then released in Nebraska in the hope that they would go to the artificial pigeon-house. A few of them seemed indeed to make their way towards it; one or two actually reached it. But statisticians denied any significance to these rare successes. They emphasized that the publicity given to the experiments ensured an unduly high chance of observations in the neighbourhood of the wrong pigeon-house.

Other experiments, conducted by Yeagley and repeated several times by other research workers, consisted of fixing tiny magnets on the wings of some pigeons, the control birds being provided with an identical non-magnetic piece of metal. The idea was to disturb in this way the magnetic field around the birds and prevent them from finding their bearings normally. The results were negative, except once. Yeagley then found that the control birds were returning to the pigeon-house long before the magnet-carriers. Even this was valueless as evidence, as the magnet-carriers had lost their magnets.

Yeagley's efforts, therefore, leave one very sceptical, though one hesitates to reject the theory completely. O. J. Stewart [18] has recently pointed out the electric conditions created by the friction of air on the feathers of a moving bird. The magnetic fields surrounding it cannot fail to react with the Earth's magnetic field and that could cause the tips of the wings to move, the movement being detectable by the bird. Stewart thinks that birds in flight might be able to correct their direction from indications given by these magnetic signals.

The experimental era

The experimental study of orientation in migrants really started in 1949, when G. Kramer [19] noticed that some starlings (*Sturnus vulgaris*) kept in a cage at the time of migration stayed mostly in that part of the cage pointing towards their normal migration route. He placed the experimental cages in pavilions from which they could not see the horizon, but could see the sun, whose apparent direction could be altered by mirrors. The birds found their bearings without landmarks as long as the sun was not hidden by cloud (figure 4). When the direction of the light rays was changed by rotating the mirrors, the birds altered their orientation (figure 5). Such experiments, and others, indicate that migrants use the position of the sun to find their direction.

According to K. Hoffmann [20], it is the azimuthal position of the sun (its horizontal projection) alone that matters. Later, G. Kramer and U. von Saint-Paul [21], followed by G. Kramer and E. Riese [22], trained starlings and pigeons to orientate themselves to a fixed direction at a given time. When the time was changed (and, consequently, the sun occupied a completely different position in the sky from that during training) the birds still turned to the original direction. Obviously, they have a notion of time that enables them to correct for solar movement. One of Kramer's collaborators, K. Hoffmann [23, 24], has proved that birds possess an internal 24-hour rhythm synchronized in some cases with local time. As an example, two starlings, trained during natural daylight to orientate themselves to a given direction, were isolated in a room and subjected to an artificial day beginning and finishing six hours later than the natural one. After some time in natural daylight, they chose a direction 90° to the right of the previous one (figure 6). This ability to allow for solar movements is inborn.

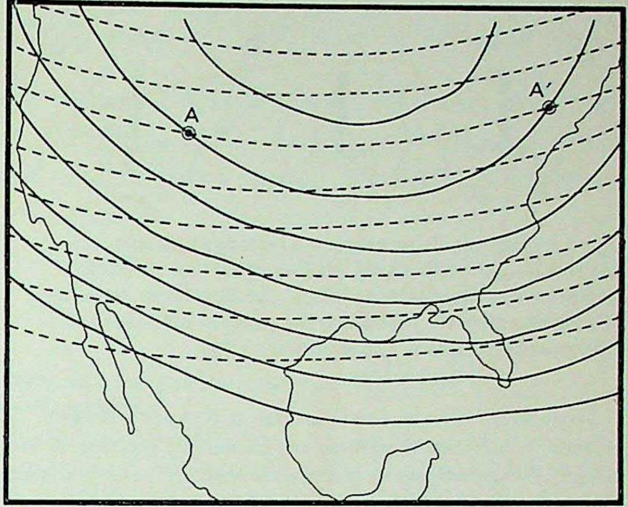

Figure 3 *Yeagley's experiment. Lines of equal Coriolis force in continuous line. Lines of equal magnetic intensity in broken line. A and A′ are two conjugate points. (After Yeagley, 1947.)*

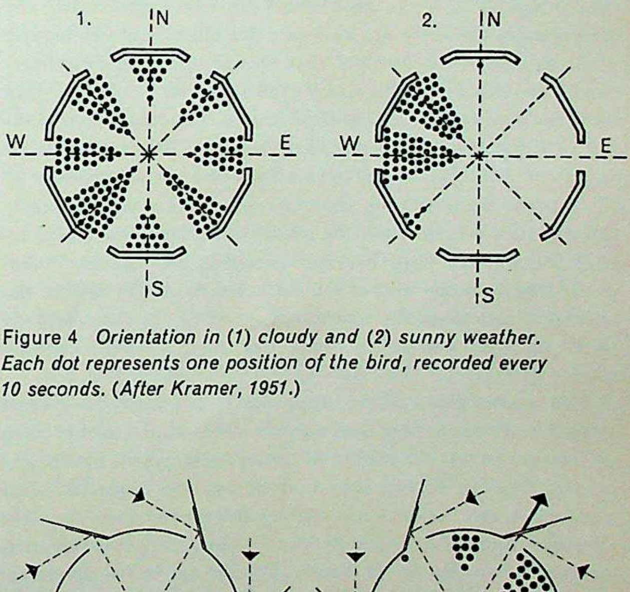

Figure 4 *Orientation in (1) cloudy and (2) sunny weather. Each dot represents one position of the bird, recorded every 10 seconds. (After Kramer, 1951.)*

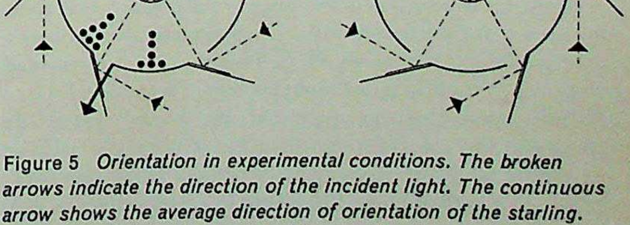

Figure 5 *Orientation in experimental conditions. The broken arrows indicate the direction of the incident light. The continuous arrow shows the average direction of orientation of the starling. Movement of the mirrors alters the direction from which the light appears to come (After Hoffmann, 1960.)*

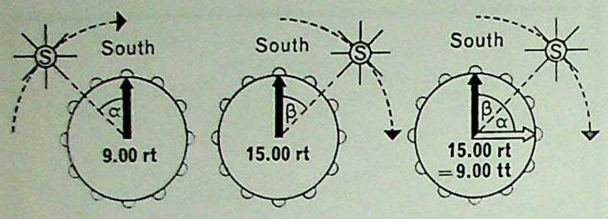

Figure 6 *Hoffmann's experiment. S represents the sun ; rt : real time (in natural daylight) ; tt : theoretical time (in artificial light of normal duration but altered). The thick arrow shows the training direction, the hollow one the direction obtained in experimental conditions.* (*After Hoffmann, 1954.*)

There are, however, inadequacies in Kramer's theories. A migrant which can determine the azimuthal position of the sun and possesses a precise internal chronometer is likely to face all sorts of problems, because the azimuthal speed of the sun varies during the day, according to the season and the latitude of the place concerned. Up to the present, no study of birds enables us to solve this problem satisfactorily. Some experiments indicate that the height of the sun, or some factor related to it, is used to give a second co-ordinate. The most interesting theory here is that of G. V. T. Matthews [28], who suggests that the bird assesses the sun's arc and uses the altitude of the highest point to give it its latitude, and an azimuthal measurement (together with a sense of time) to estimate its longitude. This view has given rise to many experiments, but runs into a number of difficulties. In particular Matthews did not make an adequate estimate of the errors involved in observations of the type he suggested the pigeons would make: more recently the accuracy which would be required has been calculated by C. J. Pennycuick [29]. Braemer considers that the interaction of the length of day and of the sun's height might enable the animal to calculate the azimuthal speed of the sun correctly in all latitudes and at all times. But this hypothesis requires confirmation.

The results given above apply only, of course, to diurnal migrants. Z. Sauer [25] used similar observation cages to those of Kramer to test the ability of nocturnal migrants (*Sylvia* sp.) to maintain an inborn direction during the night. In clear weather (when the stars are visible) the bird chooses the right direction immediately and keeps to it. But it appears to lose its bearing when the sky is cloudy. We do not know whether it is the general pattern of the sky, or that of a group of stars, or even the position of one or several stars, that matters.

Finally, let us mention a few recent results which will show how far we are yet from a satisfactory comprehensive answer to the problem of migration. H. G. Fromme [26] has recorded mechanically the orientated night activity (*Zugunruhe*) of robins (*Erithacus rubecula*) during migration. He showed that robins can choose and maintain the direction of migration without any optical landmark (consequently without being able to see the sky) in a normal room. But placed in an experimental steel room, they could no longer orientate themselves. An artificial magnetic field did not disturb them. Finally, when kept for a certain length of time in an artificial daylight altered by six hours from natural daylight, they were able to maintain their normal direction when tested in natural daylight. We must compare these observations with those of Precht and others [27] who found that *Larus ridibundus* and *L. canus* were able to orientate themselves towards their place of capture from an enclosed room with no view of the sky.

We have seen that birds are capable of orientation towards a known place from an unknown one, and are thus capable of true navigation. All interpretations of this navigation seem liable to criticism and no suggestions can be considered as proved. For the time being, therefore, the navigation of migrants remains unexplained. However, to recapitulate, we now have, despite many gaps in our knowledge, a comparatively clear idea of the mechanisms by which migrants adhere to the inborn direction.

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The physiology of sleep

Giuseppe Moruzzi

Because of its controlling influence on human behaviour, sleep has always been of profound interest. Only comparatively recently, however, has the physiological background become at all clear. This article reviews theories of the mechanism of sleep, with special reference to developments within the last five years, and discusses the significance of many experiments. The Pavlovian idea of a generalized cortical inhibition has now to be given up. It seems that in sleep there is not a decrease of cortical activity but rather a reorganization on a different basis.

In 1913, in his classic book [1], H. Piéron defined sleep as a state that is periodically necessary, with a periodicity relatively independent of the external conditions, and characterized by the interruption of the complex sensory-motor relations linking the subject to the environment. We know now that our isolation from our environment is far from complete even in the deepest sleep. Today, we have electrophysiological evidence that even during sleep, nervous impulses reach the sensory areas of the cerebral cortex from the peripheral receptors and sense organs, and that impulses travel from the motor cortex to the brain stem and spinal cord in the fibres of the pyramidal tract.

Nevertheless, the definition given by Piéron is still valid in the light of the idea of the integrative function of the nervous system put forward by C. S. Sherrington [2]. It is because of this integrative function that the multicellular organism becomes '... from a mere collection of organs an animal individual', and in sleep it is this integrated response to environmental stimuli that is profoundly impaired. It is possible to observe fragments of an integrated reaction during sleep, and in cases of somnambulism the results may well be astonishing. Nevertheless, sleep is always accompanied by an isolation, even if partial, from the environment and by the dissolution of the patterns of nervous reactions that give individual character to an animal.

In sleep, somatic and vegetative (visceral) functions have an entirely different orientation, but this seems to be a secondary element in the complex picture. The distinction made by C. von Economo [3] between sleep of the body (*Körperschlaf*) and sleep of the brain (*Hirnschlaf*) is quite apposite. The central problem is that of the sleep of the brain, and it is entirely neurophysiological in nature. We have to discover why and how the brain periodically undergoes such a profound change in its relations with the environment and in its own functional organization.

This review is confined to an analysis of the problem of sleep in the warm-blooded animals. We shall be concerned only with the problem of the neurophysiological mechanism of sleep, which has been studied more extensively and deeply than has the cause of sleep. We shall see that all worth-while experiments and ideas on the mechanism of sleep lead eventually to two main working hypotheses, namely, that sleep is due to deafferentation or to inhibition. The first two sections of this review will summarize these ideas. The third will re-examine, in the light of the advances made in the last five years, theories that have so far been put forward.

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Was born in 1910 and was educated at the University of Parma Medical School. He was appointed acting head of the Physiological Laboratory in the Universities of Siena (1942) and Parma (1945), and became Professor of Physiology at the Universities of Ferrara (1947) and Pisa (from 1948). He has published extensively on the physiology of the cerebellum and of the reticular formation.

Sleep as a passive phenomenon: the theory of deafferentation

The basis of this conception is the idea that it is not necessary to postulate the existence of a centre for sleep. Sleep is simply the end of the waking state and therefore is, in a way, a passive state. It is not necessary to pose the question of whether there is a sleep centre in the brain: the central problem for the physiologist is that of recognizing the parts of the central nervous system that are necessary to maintain the state of wakefulness. Partial or complete suppression of the activity of these nervous centres, brought about by the reduction of the afferent impulses that maintain their tonic activity, is sufficient to abolish wakefulness and thus to produce sleep.

It appears that K. F. Burdach [4] was the first to formulate this idea, but its first clear and complete expression is found in the chapter on sleep which J. E. Purkinje wrote for R. Wagner's *Handwörterbuch der Physiologie* [5], a few years after the discovery by P. Flourens [6] of the sleeping attitude produced in the pigeon by removal of the cerebral hemispheres. Purkinje's ideas were developed by D. Mauthner [7]. To N. Kleitman [8, 9] we owe the most complete and exhaustive formulation of the theory of deafferentation and to F. Bremer [10] its experimental demonstration.

The fundamental work of Bremer was on the *cerveau isolé* preparation; a diagram of this experiment for the cat, giving also the relevant anatomical nomenclature, is shown in figure 1. The encephalon comprises the neural structures within the skull. It consists of three parts: an anterior portion (the cerebrum), a posterior portion (the cerebellum), and the brain stem. The cerebrum may be divided into the telencephalon (which includes the cerebral cortex) and the diencephalon (thalamus, subthalamus, and hypothalamus). The brain stem is divided into three parts: medulla, pons, and midbrain. When

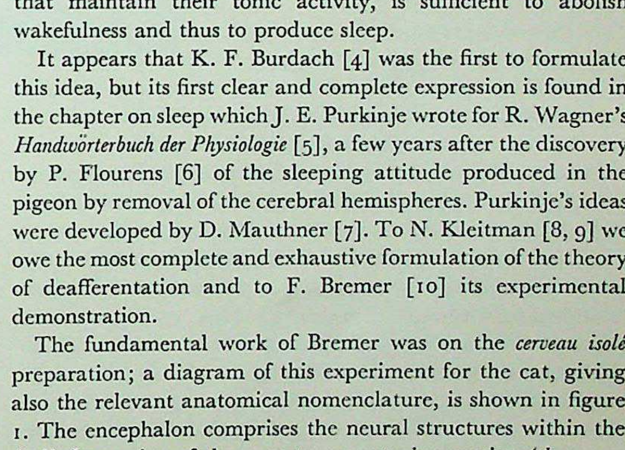

Figure 1 *Principal structures in the encephalon of the cat, with special relation to the* cerveau isolé *preparation.*

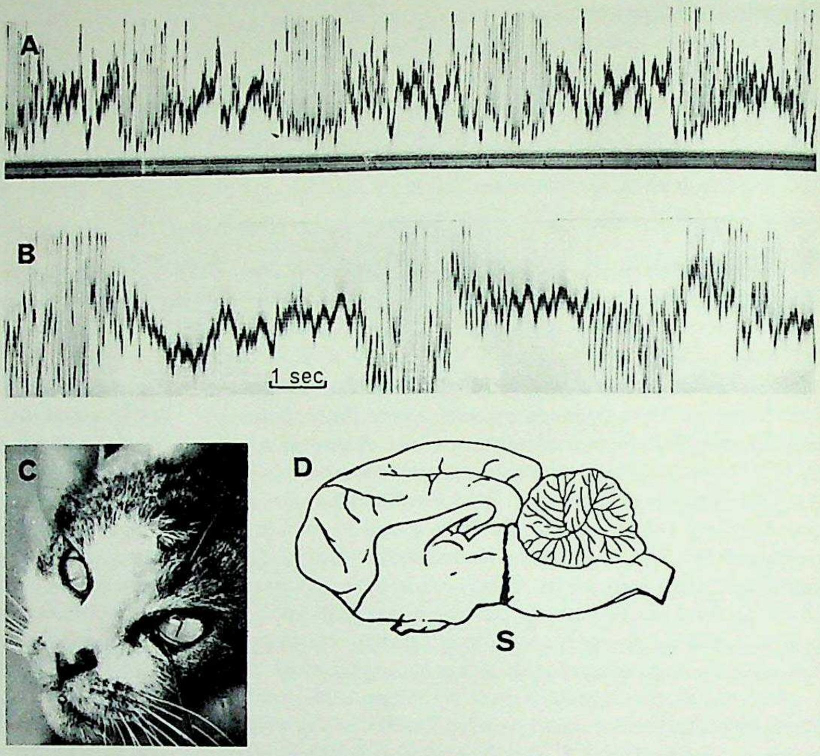

Figure 2 *Behaviour of the eyes and E.E.G. record of the* cerveau isolé *preparation of the cat. A postcollicular mesencephalic transection (S) causes narrowing of the pupil (myosis) to a fissure-like slit (C). At the same time there is the typical E.E.G. pattern of deep sleep, with high-voltage waves (spindles) with interposed periods of low-voltage activity (A). There is a remarkable resemblance between this E.E.G. pattern and that of barbiturate anaesthesia in the intact cat (B). (From [11].)*

a transection is carried out at the level of the mesencephalon (1 in figure 1), the cerebrum is isolated from the rest of the encephalon. This preparation was called *cerveau isolé* by Bremer. The anterior part of the midbrain is still attached to the cerebrum, and the oculomotor nucleus—which innervates most of the external ocular muscles and the pupillo-constrictor muscle—is the only efferent system permitting expression of behaviour in this preparation.

A more caudal transection (midpontine pretrigeminal preparation), carried out in the middle of the pons in front of the trigeminus nerve (2 in figure 1), gives rise to a preparation with the same afferent (olfactory and optic) and efferent (oculomotor) pathways, but characterized by different physiological properties. The brain-stem reticular formation is situated in the core of the brain stem, extending from the medulla through the midbrain. The ascending projections of these neurones (ascending reticular system) exert a widespread influence on the cerebrum. This system is also called a diffuse projection system, as opposed to specific afferent systems which extend to well-defined areas of the cerebral cortex, such as the lateral lemniscus, which is involved in somatic sensation.

If the brain stem of the cat is separated from more caudal levels of the nervous system by a complete transection performed at the level of the mesencephalon, the electroencephalogram has all the characteristic features found also in deep sleep. Trains of high-voltage waves, called spindles, alternate with periods in which the tracing shows only low-voltage activity. As the section is usually performed caudally to the emergence of the oculomotor nerve from the mesencephalon, the ocular behaviour of the animal may also be observed. It is found to be typical of deep sleep, in that the pupils are narrowed down to a fissure (fissurated myosis) and the eyeballs take up a characteristic position of rotation (figure 2). This observation is evidence for the theory of deafferentation [11]. The fact that the isolated brain sleeps is 'the result of the interruption of the afferent pathways to the cortex and consequent suppression of the continuous inflow of afferent impulses, above all from the skin and proprioceptive end organs; such impulses are essential for maintaining the telencephalon in a state of vigilance, as the olfactory and visual organs are clearly not capable of doing so'. Bremer stressed the fact that physiological sleep is not induced merely by the functional deafferentation of the cerebral cortex. It had already been known for some time that sleep and wakefulness appear to occur even in the decorticate mammal. Bremer has pointed out that the continuous inflow of impulses from external and proprioceptive end organs also helps to maintain the manifestations of wakefulness by means of a direct action on the diencephalon. The diminution in tone of the cerebral cortex and of the diencephalon frees the oculomotor nucleus from an inhibitory action, thus producing narrowing of the pupil.

The further development of the theory of deafferentation came from investigations of the ascending reticular formation. It is well known that electrical stimulation of the reticular formation [12] causes the same electroencephalographic picture of the alert state (figure 3), and that this effect is due to impulses that reach the cortex through pathways different from the lemniscal tracts (figure 4). From this result originated the conception that it is the tonic activity of the ascending reticular formation that maintains wakefulness [12]. This hypothesis can explain facts that the classical theory of deafferentation cannot. Thus, without it we would not be able to explain the sleep of encephalitis in which there are lesions in the central grey matter and in the mesencephalic tegmentum [7, 13] and the comatose states caused by lesions of the hypothalamus [14]. The state of sleep of the *cerveau isolé* preparation is due, according to this later hypothesis, to the interruption of the mesencephalic tegmentum and not to a break in the lemniscal pathways [12]. This new hypothesis can be easily put to a crucial test. It is found that the same electroencephalographic and behavioural patterns as occur in the *cerveau isolé* preparation may be reproduced by means of a lesion of the mesencephalic tegmentum not encroaching on the lemniscal pathways [15]. On the other hand, a complete section of the lemniscal fibres alone does not cause coma (figure 5), even if it is not without effect [16]. Chronic

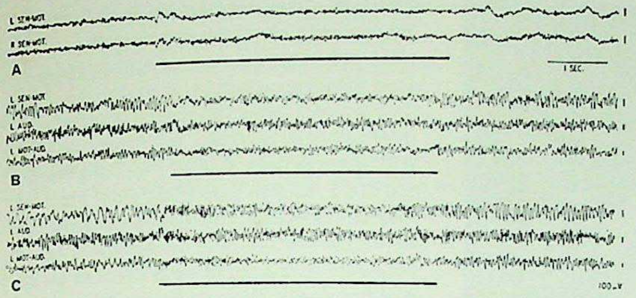

Figure 3 *Effects of the electrical stimulation (300/sec) of the reticular formation of the brain stem of the cat. The period of stimulation is indicated by the heavy horizontal line. The E.E.G. arousal reaction does not occur when there is an activated E.E.G. pattern (A), but it is evident when the pattern is synchronized (B, C). (From [12].)*

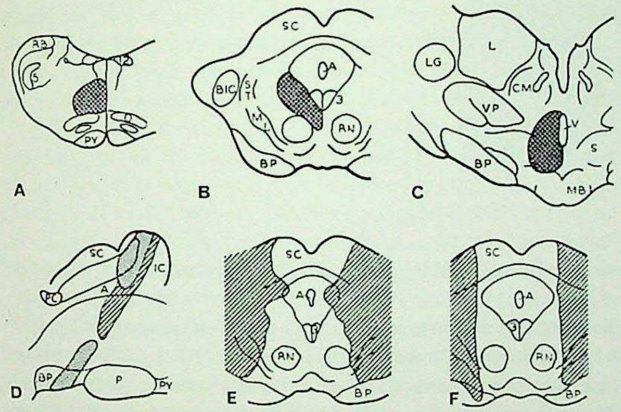

Figure 4 *Ascending pathways of the reticular system of the cat. A, B, and C are sections of the bulbar, mesencephalic, and diencephalic areas respectively from which an arousal reaction may be obtained with low-voltage stimulation (frequency 300/sec). In the transverse sections at mesencephalic levels (E, F) the shaded areas indicate the extent of the lesions, which cut across the classical afferent pathways (lemnisca) without abolishing the E.E.G. changes brought about by electrical stimulation of the reticular formation of the bulb. In the sagittal section at mesencephalic level (D) the dotted areas indicate the regions whose destruction does not abolish the E.E.G. changes resulting from stimulation of the reticular formation; these changes do not occur when the lesion covers the shaded areas. (From [12].)*

lesions of the mesencephalon in the cat and in the monkey [17, 18] support this conclusion.

We can summarize these investigations by saying that it has been experimentally established that complete interruption of the ascending reticular system causes states similar to those of coma and lethargic sleep. It follows that physiological sleep is due to a moderate and reversible decrease of this tonic activity. If we accept this hypothesis, we must radically modify the classical theory of deafferentation, but at the same time this fundamental idea is strengthened. Wakefulness seems to require a critical level of tonic activity in the ascending reticular system; a reduction of this level of activity is, in a way, equivalent to the deafferentation of the brain, and causes sleep simply because it is incompatible with wakefulness. We can therefore explain why in sleep afferent impulses can still reach the sensory areas of the cortex in which the specific projection systems end. From this physiological hypothesis derive new ideas in the field of pharmacology, in regard to barbiturate-induced sleep, and in pathology, in relation to coma. A recent review [19] gives an extensive bibliography on this subject.

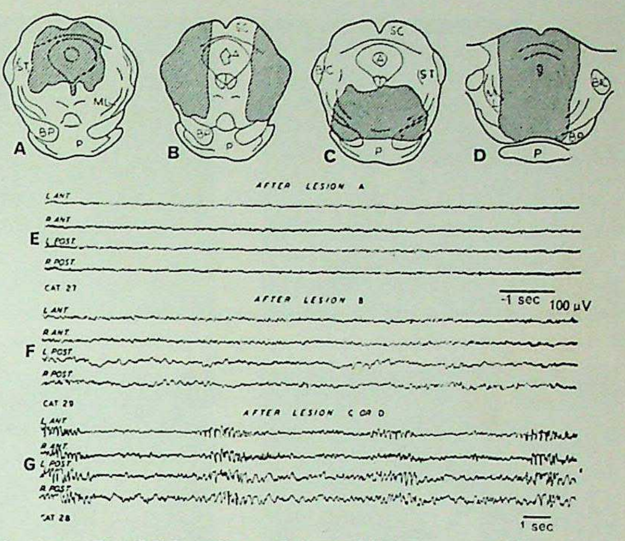

Figure 5 *The E.E.G. pattern of sleep of the* cerveau isolé *preparation may be obtained with lesions of the mesencephalic tegmentum with (D) or without (C) simultaneous lesions of the central grey matter. Isolated lesions of the central grey matter (A) or of the lateral areas impinging on the main sensory pathways (B) do not have such an effect. (From [15].)*

Old findings and ideas may be reinterpreted in the light of the reticular hypothesis. The centre of wakefulness which Purkinje had postulated may be identified with the ascending reticular system, but the cerebral cortex may help to maintain its tonic activity by the continuous flow of impulses in the cortico-reticular fibres, whose existence is now well documented, both anatomically and physiologically [19]. The exceptional proneness to sleep of the newborn mammal may be due to the absence of the cortical influence on the ascending reticular system. Even the behavioural sleep which Flourens [6] induced in the pigeon by removing the cerebral hemispheres is linked to the suppression of the action of the cerebrum—even though almost completely devoid of cortex—on the brain stem. The fleeting behavioural signs of wakefulness, which can be obtained in these conditions [20] with different kinds of sensory stimulation, are merely transient manifestations of arousal.

Sleep as an active event: the inhibition theories

Here we do not find the same unity of thought as in the theory of deafferentation, though no doubt there is an element common to all hypotheses. The main point is not how wakefulness is maintained, but how sleep is produced. This is considered to happen because of an active mechanism, brought about by specific structures [24–26] or, at least, by a definite temporal and spatial pattern of afferent impulses [22]. These active mechanisms are often thought to be inhibitory, in accordance with the prevailing idea that sleep is a state of inactivity, or at least of decreased activity, of the nervous centres.

The theory of inhibition was first formulated, although rather loosely, by C. E. Brown-Séquard [21]. There are two main trends of thought in this field, one of them headed by I. P. Pavlov and the other by W. R. Hess.

The basis of Pavlov's idea is the observation [22] that sleep is frequent in the course of conditioning experiments when the conditioned response is extinguished. This is attributed to a process of localized, or internal, inhibition, which under favourable conditions could spread to the whole of the brain—both to the cortex and to the subcortical centres—thus causing sleep. The observations and ideas of Pavlov have been critically examined elsewhere [23]. The phenomenon is genuine,

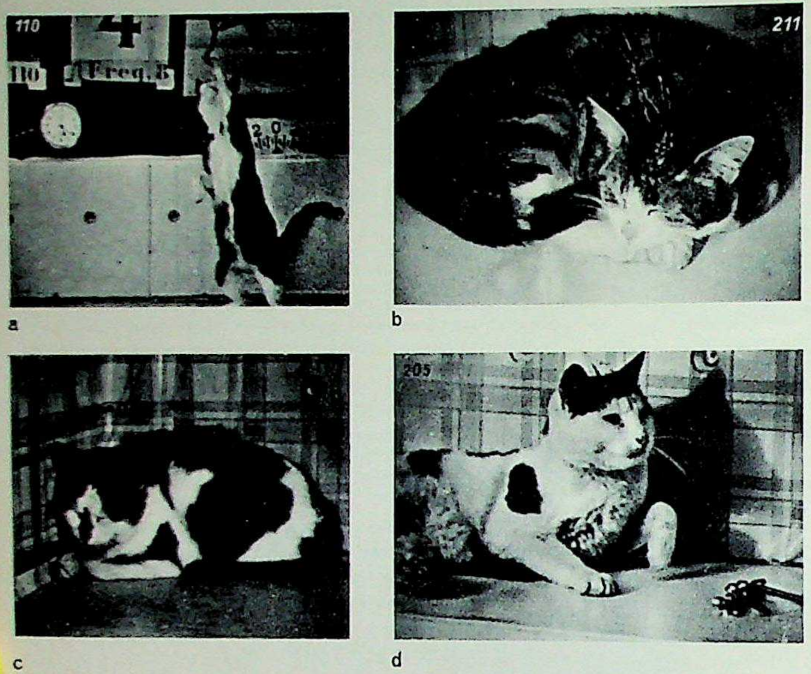

Figure 6 *Sleep reaction obtained by Hess. The cat with permanently implanted electrodes shows a normal behaviour* (a). *Low-frequency electrical stimulation (2–4 per sec), repeated several times at intervals of 30 seconds, is followed by typical physiological sleep* (b). *Occasionally the same reaction may result from the mechanical stimulation due to the insertion of the stimulating electrode in the hypnotic zone* (c). *This sleep is perfectly reversible, and the animal is easily awakened, as by the noise produced by dropping a bunch of keys* (d). *(From Hess [26].)*

although it should be stressed that, if repeated monotonously, any stimulus may cause sleep, quite independently of conditioning experiments. Pavlov's theories have not been helped by the vagueness of the anatomical terminology. Kleitman [9] has rightly pointed out that there can be no inhibition without activity of the inhibiting centres, which are not considered in Pavlov's theory. But even if sleep were not the consequence of repetition of an inhibitory process, the fact is that a characteristic spatial and temporal pattern of afferent impulses may produce sleep. It seems extremely improbable that this would happen if volleys of afferent impulses do not act on some central organ, which is thereby gradually stimulated into activity [23]. This automatically implies the existence of sleep-producing centres, and the idea that sleep appears when these centres become active because of reflex or humoral mechanisms.

This is the only link between Pavlov's and Hess's theories. The experimental basis of the latter is the production of sleep in the normal cat by low-frequency stimulation of given regions of the diencephalon or mesencephalon. This kind of sleep is entirely similar to physiological sleep (figure 6), as can be seen from the posture of the animal, the possibility of awakening it, and the electroencephalographic pattern. The areas stimulated by Hess belong to his trophotropic system, whose function is to restore the energy of the organism. This system is opposed by an ergotropic system, mediating energy expenditure in attack and in defence, and the reticular ascending formation is part of it [25]. This dualistic conception of two antagonistic centres governing the periodic rhythm of sleep and wakefulness had been previously advanced by von Economo [3] and W. J. H. Nauta [27].

I would like now to recall the distinction made by von Economo [3] between sleep of the brain and sleep of the body. There is no doubt that many somatic and vegetative phenomena of sleep are linked to central activities which are inhibitory in nature. Let us consider, for instance, the classical experiment of J. Tarchanoff [28], which shows that after section of the spinal cord at a thoracic level in the dog, reflexes evoked during sleep by electrical stimulation of the skin are greatly depressed in the forelegs, while they are unaffected in the hindlegs. It is impossible to explain such observations without postulating that some reflex functions are subjected to supraspinal inhibitory influences during sleep. It is very likely that such inhibitory influences may originate in the inhibitory bulbar centre discovered by H. W. Magoun and R. Rhines [29]. The same hypothesis may be valid in the case of the relaxation of the neck muscles [30] and for the cataleptic periods that have been observed by P. Bard and M. B. Macht [31] in the decerebrate preparation.

But all these examples of sleep of the body do not prove that sleep of the brain is due to the action of an inhibitory centre. Hess points out quite rightly [25] that some somatic and autonomic manifestations, such as the contraction of the orbicular muscle of the eyelids and pupillary constriction during sleep, indicate that tonic activity increases in sleep in some other neurones. In fact, the changes that occur because of the sleep of the body may result in making deeper the sleep of the brain, by progressively reducing the inflow of sensory impulses. It is very unlikely, however, that they are the cause of it. It is interesting that the postural changes usually occurring in sleep may be dissociated from the sleep of the brain, as is shown by clinical cases of catalepsis and periods of atonia in the decerebrate preparation. It is significant that fragments of sleep behaviour—but not real sleep—are seen in the decerebrate animal, because this means that some circuits may still be operative, even in the absence of the brain. These observations cannot be adduced, however, in favour of the theory of inhibition.

Recent research on the physiology of sleep

Up to now, I have reviewed our knowledge of the physiology of sleep as it would have appeared to us in 1957, and will now try to summarize the advances made in the last five years. This separation of the old from the new is justifiable, because the new findings compel us to revise some ideas that were thought to be well founded. One has the impression that we are once again at a turning point in the history of the ideas on sleep of mammals. I will restrict this survey to two topics: centres of the caudal brain stem antagonistic to the ascending reticular system, and sleep without cortical synchronization.

Investigation of bulbar and pontine centres antagonistic to the ascending reticular formation originated in the observation [32, 33] that the picture of continuous sleep in the *cerveau isolé* preparation does not occur with the mid-pontine pretrigeminal section described earlier. The electroencephalographic tracing of this preparation shows only rarely the trains of high-voltage waves that are considered to be the result of synchronous pulsations of cortical neurones and are characteristic of physiological sleep and of the *cerveau isolé* preparation. Such an E.E.G. pattern is described as desynchronized or activated, because it is similar to that of the animal when awake. Indeed, when the E.E.G. pattern is desynchronized there is often, but not always, an alert behaviour. The eyes follow an object moving in the visual field in the vertical plane, and it is possible to inhibit the pupillo-constrictor neurones of the oculomotor nucleus, and obtain mydriasis (enlargement of the pupil) as part of the orientation reflex or as an effect of conditioning [34]. These manifestations of behavioural wakefulness cannot be observed when the tracing is synchronized, that is, when there are trains of slow waves that correspond electroencephalographically to sleep. These periods of synchronization cover not more than 10–35 per cent of the tracing, whereas in the normal cat, in a quiet and warm environment, they cover about 50–80 per cent of the recording time. This may indicate [32, 33] that caudally to the level of the transection there may be centres acting on the cerebral cortex that cause synchronous patterns and therefore act in opposition to the ascending reticular formation (figure 7).

These centres are located in the bulb or in the caudal part of the pons, as may be shown in experiments in which specific pharmacological inactivation is used [35]; or localized electrical stimulation is carried out [36]; or E.E.G. asymmetries, brought about by hemisection of the brain stem, are obtained [37].

M. Bonvallet and V. Bloch [38] have reached the same conclusions, after having seen that the activation in the E.E.G. due to stimulation of the reticular formation in the mesencephalon is of shorter duration in the *encéphale isolé* preparation with high cervical transection than in the preparation in which the bulb has been cut off from the remainder of the encephalon.

The bulbo-pontine synchronizing centres might act by inhibiting the ascending reticular formation or by stimulating the activity of the diencephalic centres studied by Hess [24–26] and by R. S. Morison and E. W. Dempsey [39]. In physiological conditions the activity of these bulbar and pontine centres might be brought about by fibres descending from the cortex or by ascending pathways mediating somatic and vegetative sensations. Pavlovian sleep, and sleep produced by monotonously repeated sensory stimulation, might be linked to the activity of these synchronizing centres [23].

Although occasional preliminary observations may be found in earlier papers, the systematic study of sleep accompanied by an E.E.G. record entirely similar to that of wakefulness begins with the observations of W. Dement and N. Kleitman [40] and of Dement [41]. Up to now, these investigations have been carried out in man and in the cat. In man, the periods of sleep with desynchronized E.E.G. pattern have been attributed to dreams. In the cat, on the other hand, desynchronized sleep is deeper than that which occurs when there are in the E.E.G. record trains of waves that were considered to be the only, or at least the main, electroencephalographic sign of sleep. Recent and very extensive reviews [30, 42] make superfluous a detailed analysis of this phenomenon. The most interesting aspects of this work are the results of microelectrode recordings from single cortical neurones [43] and reticular neurones [44] in the intact unanaesthetized cat.

D. G. Whitlock, A. Arduini, and G. Moruzzi [45] have found that single pyramidal fibres that discharge at every synchronous wave of sleep appearing on the motor area [46], rather unexpectedly stop discharging when there is arousal and the E.E.G. record becomes activated (figure 8). These observations were made without anaesthesia, but cortical synchronization was obtained by transecting the mesencephalic tegmentum. E. V. Evarts [43] has also observed this fact, which may at first appear paradoxical. Nearly half the units recorded—and, more precisely, all units which in the awake animal discharge with a frequency below 8 per sec—increase the frequency of their spontaneous discharge during sleep. Another result not predictable on the basis of the inhibitory theories is that the suppression of discharge in cortical units due to a volley of centripetal impulses may be more prolonged during wakefulness than during sleep.

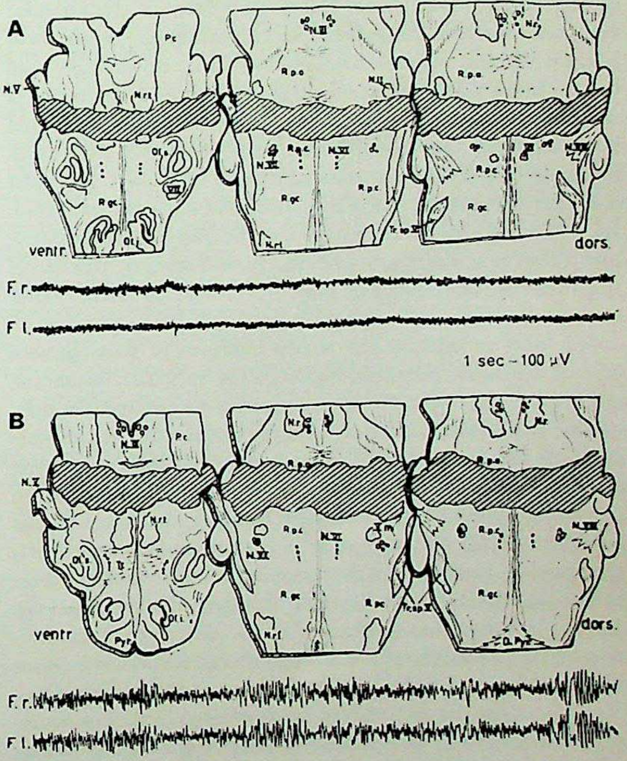

Figure 7 *E.E.G. tracings recorded after midpontine (A) and prepontine transections (B). The tracings recorded from the right and left frontal lobes (F.r., F.l.) have the pattern found in the* cerveau isolé *preparation only when the transection is prepontine at a level between the pons and the mesencephalon. (From [33].)*

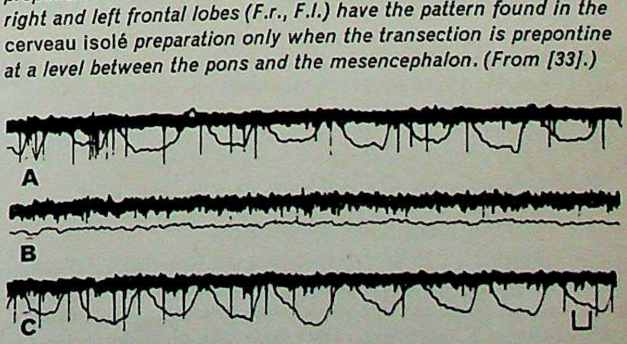

Figure 8 *Disappearance of the synchronized pattern and of the corresponding activity in the pyramidal tract (A) during activation of the E.E.G. pattern (B). A: spontaneous activity following section of the mesencephalic tegmentum. B: 10 seconds after olfactory stimulation (arousal reaction). C: 60 seconds after B (the synchronized pattern is returning). (From [45].)*

These observations make untenable the Pavlovian idea of a generalized cortical inhibition. But even the view that sleep may represent a uniform decrease of the cortical tone owing to decreased reticular activating tone cannot easily be reconciled with Evarts's observations. In sleep, there is not a disappearance of cortical activity but rather a reorganization on a different basis. This does not mean that the brain as a whole is active; it definitely shows, however, that the tiny part of the brain that has been explored so far is not resting in its entirety.

The supporters of the inhibition theory of sleep suppose that the sleep-inducing inhibition acts mainly on the neurones of the ascending reticular formation. This view is not supported by the results obtained by P. R. Huttenlocher [44], but it must be emphasized that neither is it refuted by them. There is no doubt that in the reticular formation there is a small group of units discharging with a frequency higher than 15 per sec, which increase their activity during wakefulness and decrease it during synchronized sleep. But the majority of the reticular neurones behave in the opposite way. Furthermore, when there is sleep without synchronization—which is, as we have said before, much deeper than synchronized sleep—23 units out of 28 double the frequency of their impulses compared with that in wakefulness. Obviously, it may be objected that these units do not belong to the reticular activating formation. We must also take into account that during sleep without synchronization there occur spasms of the muscles of the eyes and of the body, and there is a suspicion that the high-frequency discharges recorded by Huttenlocher may be related to these motor phenomena.

It is easy to criticize the results obtained in investigations carried out with microelectrodes in the reticular formation, although it may be difficult to suggest a way round the difficulties. It is clear that unitary analysis of the reticular neurones demands their preliminary functional identification and their classification in one of the three major groups known so far: activating systems, synchronizing systems, and the reticulospinal system for the regulation of posture and movements. It is surprising, nevertheless, that even in the cerebral cortex there are no signs of an overall decrease of activity during sleep [43]. Recent investigations on the pyramidal discharge in the free-moving, unanaesthetized cat actually show a surprising increase of the corticofugal barrage of the motor cortex at the onset and throughout the desynchronized phase of sleep [47]. For neurophysiologists it may be stimulating, but also chastening, to have to admit that after a quarter of a century of intense, and often lucky, work we are not yet able to explain the meaning of the popular saying 'a refreshing sleep'.

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Luminescence in animals

J. A. C. Nicol

Luminescence occurs widely among animals—it exists in more than half of the zoological phyla. Among these animals, it is produced in widely varying organs, using very diverse substances. Its function is clear in some cases, such as the fireflies and some deep-sea fish, but obscure in others. This article discusses the biochemistry and physiology of animal luminescence in a number of different cases, and also the possible value of luminescence to the animal.

The production of light by organisms, bioluminescence, is one form of chemiluminescence; the term refers to the emission of light during a chemical reaction that does not involve heating to incandescence. The reaction is exothermic and is usually an oxidation. Chemical energy is expended in raising some potential light-emitter to an excited state, and when the energy of the molecule falls to a state of lower energy, light is emitted.

Occurrence of luminescence among animals

Luminescence is very widespread among animals, occurring in over one-half of the major groups or phyla recognized by zoologists, from single-celled protozoans to fishes; these latter are the only group of vertebrates having luminous representatives. Luminous species are chiefly marine or terrestrial and are very rare in fresh water. Although luminescence appears to be most abundant among marine animals, it is likely that these are equalled in number by species of terrestrial fireflies that abound in tropical regions. However, for diversity of luminous organs and modes of light-emission we must go to the sea. Luminous species are especially noteworthy among coelenterates, such as jellyfish and ctenophores or comb-jellies; crustacea, such as prawns; and squid and bony fishes. It is in the three latter groups that luminous organs attain the greatest complexity.

On land, luminescence is found in nocturnal animals such as fireflies and in animals inhabiting dark places such as fungus-gnats. In the sea there are many luminous animals that live in surface waters, such as flagellates (microscopic cells) and comb-jellies, but luminescence is especially characteristic of animals that live in the dimly lit or dark depths of the ocean. In an extensive survey off Bermuda, W. Beebe [1] found that two-thirds of all species of fish captured below 550 m were luminescent; estimated as individuals, over nine-tenths were luminous. Apart from fish, we must take into account the vast numbers of luminous jellyfishes, copepods, prawns, and squids that inhabit the deep waters of the oceans.

By sending down photomultipliers protected against implosion, G. L. Clarke and colleagues have been able to record levels and patterns of luminescence in different places and at different depths. Their records show intermittent, sometimes almost continuous, bursts of luminous flashes, both in surface waters at night and in deep waters by day and night (figure 1). The energy levels in these flashes attain 10^{-7}–10^{-3} μW falling on one cm² of receptor surface [2]. Such intensities are easily visible to animals, and it has been surmised that these summated flashes may form a continuous background illumination that is bright enough for visual purposes. However, the photomultiplier itself is a disturbing factor, and animals probably strike against the casing; until the problem is resolved, it is difficult to estimate the degree of normal or spontaneous luminescence that occurs in deep waters.

Luminous organs

Light-production in animals occurs in three ways. It takes place within cells—intracellular luminescence; or a luminous secretion is discharged—extracellular luminescence; or the light is produced by luminous symbiotic bacteria within the animal. Usually an animal shows only one kind of luminescence, but there are species, such as prawns and fish, exhibiting both extracellular and intracellular luminescence.

Extracellular luminescence occurs in many animals, including polychaete worms, bivalve molluscs (such as *Pholas*), squids (such as *Heteroteuthis*), and bony fishes (such as *Searsia*). The glandular cells that discharge the secretion may form a single epithelial layer on the surface of the animal or be arranged in subsurface sacs that discharge through ducts. Sometimes there are two types of cells present, which may represent the sites of manufacture of luciferin and luciferase, as in copepods and ostracods (small marine crustaceans related to prawns). In squids, the secretion is produced in a gland adjoining the ink-sac, and it is discharged into the mantle cavity and expelled through the siphon.

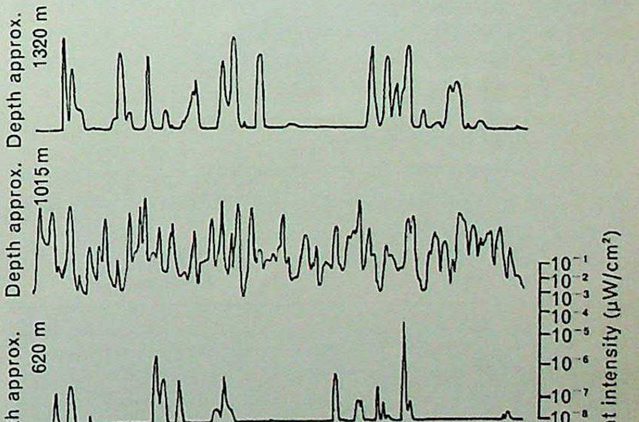

Figure 1 *Records of ambient light-levels and luminous flashes in the ocean, as detected by a submerged bathyphotometer in the western North Atlantic at 38° 38′N, 69° 09′W, 13th August 1959. Total water depth to bottom, 3658 m. Upward inflexions correspond to flashes of animals. On this occasion a greater degree of flashing was encountered at 1500 m than at levels above and below this; frequently, at the greater depths, fewer flashes are found and many of them are extremely prolonged. (Record supplied by Professor G. L. Clarke of the Wood's Hole Oceanographic Institute.)*

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Organs concerned with intracellular luminescence are much more varied and often attain great complexity. In their simplest form, they are mere plaques of luminescent cells. Among scale-worms (figure 2), for example, each luminous patch consists of a single layer of modified epidermal cells. The luminous areas of some jellyfish correspond to small masses of epithelial cells in the walls of the circulatory canals. Again, in some deep-sea shrimps, such as *Sergestes*, the liver or digestive gland may contain a luminous lobe, and the luminous glands of certain gnats (Bolitophilidae) are derived from fat bodies or excretory tubules. When luminous glands are internal, as in these instances, the light must traverse the translucent body wall of the animal before reaching the exterior [2].

Complex light-organs that contain accessory structures increasing their efficiency are found in deep-sea squids, prawns, and fishes (figures 4 and 5). Usually these organs are cup-shaped and are built somewhat like a bull's-eye lantern. The outside of the cup is covered with a dense screen of pigment and the inside is lined with a layer of reflecting tissue (figure 7). Within the cup lies a mass of light-producing cells or photocytes, and the front of the organ often contains one or several lenses affecting the dispersion of the light beam. The reflector is responsible for the glitter or iridescent sheen that light-organs often exhibit. Unfortunately, apart from its appearance, little is known about its composition or optical characteristics. The reflector of fireflies is supposed to contain crystals of a urate; and that of fish, platelets of guanin, the material that is responsible for the iridescent or white appearance of fish scales [3, 4].

When symbiotic bacteria are involved in luminescence, they are housed in special sacs or gland-like organs, variously disposed. Squids have a pair of bacterial light-organs that fit into the ink-sac, and the interior is subdivided into compartments containing luminous bacteria. A reflector and lens are present, and the ink forms a light-absorbing screen (figure 8). In fishes, the bacterial organs lie in most diverse situations, such as the ventral body wall, the lower jaw, or the wall of the oesophagus or intestine; sometimes the organs are provided with reflectors and are backed by black screens. When the light-organs are deep-seated, as are those within the abdominal cavity of fishes, the light escapes over a wide area of the body wall and has a very diffuse character [4].

Regulation of light-emission

Rarely, light-emission is continuous, as it is in the deep-sea squid *Spirula* and the millipede *Luminodesmus*. In the great majority of animals, light-emission occurs intermittently, either spontaneously or in response to some external stimulus. Flashes vary greatly in duration, ranging from 0·1 sec in single-celled protozoans (*Polyedra, Noctiluca*) to 1 sec in jellyfishes, and 20 sec or so in euphausiids (small shrimp-like creatures) and squids. Sometimes animals flash repetitively, thereby prolonging the response (figure 3) [2].

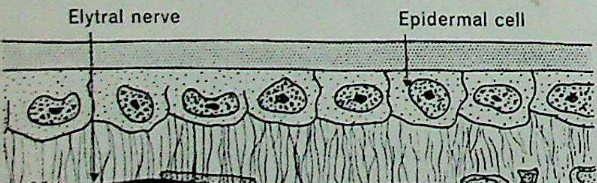


Figure 2 *Structure of the scale of a polynoid or scale-worm, as seen in vertical section.*

The animals just mentioned produce light intracellularly. Extracellular luminescence is often protracted, lasting a few seconds in squids, copepods, shrimps, and fish, and up to five minutes in the paddle-worm *Chaetopterus* (figure 3) [2]. The flashes of copepods are noteworthy because of the rapidity with which the response begins. The latent period between stimulus and the appearance is only some 10 msec, and maximal flashing is reached in 30 msec (figure 3). These times are within the range found in some of the fastest intracellular flashes, and raise the problem of how the animal manages to expel a luminous secretion so quickly [5]. Organs containing luminous bacteria are continuously luminous, although there may be devices for varying the intensity or for screening the light.

The responses of muscle to nervous stimulation have long been used as indices of nervous functioning, and the luminous flashes of animals have been employed in the same manner to yield information about events in that part of the nervous system regulating the luminous organs. The most primitive animals with nervous systems are the coelenterates, of which the sea-pens or pennatulids (figure 6) are notable luminous representatives. A sea-pen is a colonial animal containing many individual polyps, each of which is capable of flashing. When a sea-pen is stimulated, a wave of light ripples across the surface of the animal as individual polyps light up successively. The flash of each polyp lasts about 0·2 sec; the wave of light is propagated at a velocity of 5 cm per sec; and the whole response lasts about 1 sec (figure 3). Luminescence can be elicited by touching any part of a sea-pen and is transmitted in any direction across its surface. The nervous system of a sea-pen is organized as a pervasive network, consisting of many linked nerve cells capable of passing nerve impulses with equal facility in either direction from one nerve cell to another. Moreover, the network allows through-transmission, so that an impulse, initiated in this system, courses throughout its ramifications without hindrance and excites all the light-generating tissue of the animal [2].

In scale-worms, to pass to a more complex animal, there is a

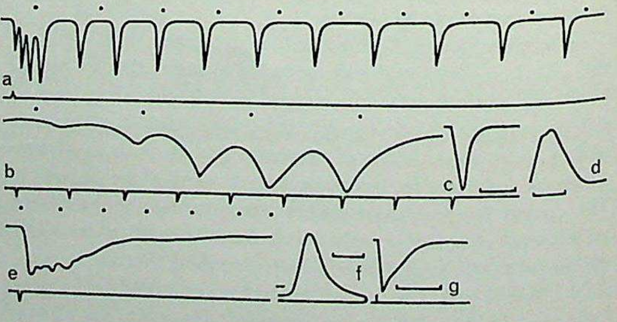
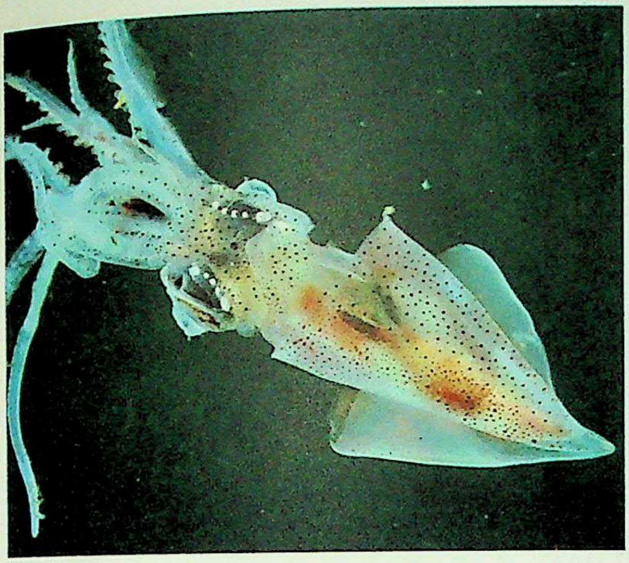


Figure 3 *Photoelectric recordings of the light-flashes of animals. The excursions represent luminous flashes. Flashing induced by electrical stimulation (shown by marks on the lower line) in all records except (d), (a), scale-worm* Acholoë astericola. *(b), sea pansy* Renilla köllikeri *(a pennatulid). (c), single-celled animal,* Noctiluca miliaris. *(d), firefly* Photinus pyralis. *(e), paddle-worm* Chaetopterus variopedatus. *(f), comb-jelly* Mnemiopsis leidyi. *(g), copepod* Metridia longa, *a minute crustacean allied to shrimps. Time in secs:* (a, g), 1; (b), 0·8; (c), 0·01; (d, f), 0·1; (e), 30.



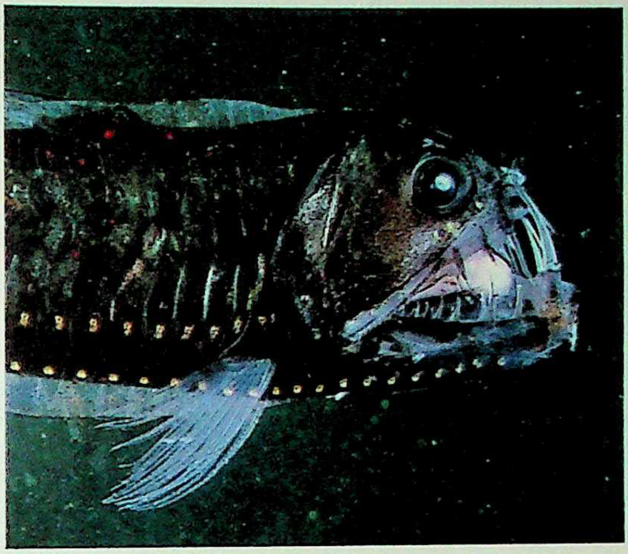
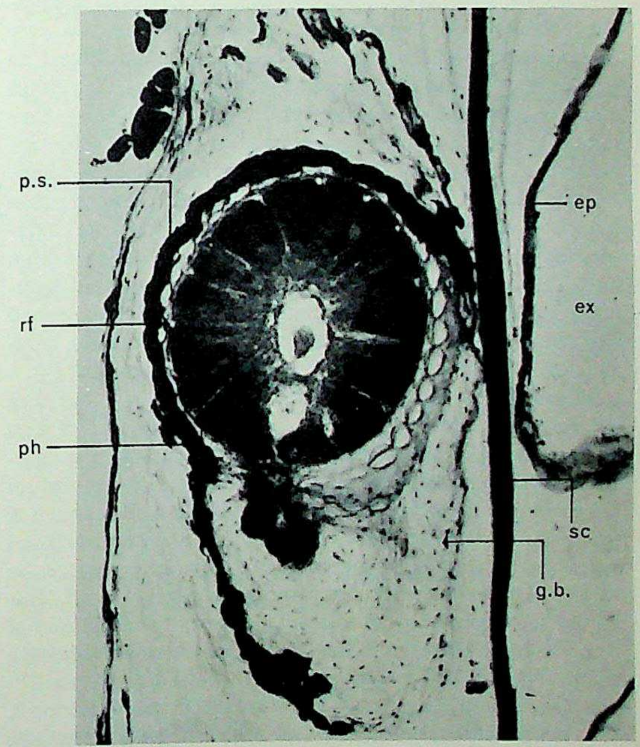


Figure 4 *A pelagic squid* Abraliopsis *with photophores around the eyes. Ventral view. This animal is about 7 cm long. (Photographs 4 and 5 by P. David.)*

Figure 5 (above, right) *A deep-sea fish,* Chauliodus sloani. *There is a violet light-organ beneath the eye and serial photophores along the trunk and beneath the jaw. (× 2 approx.)*



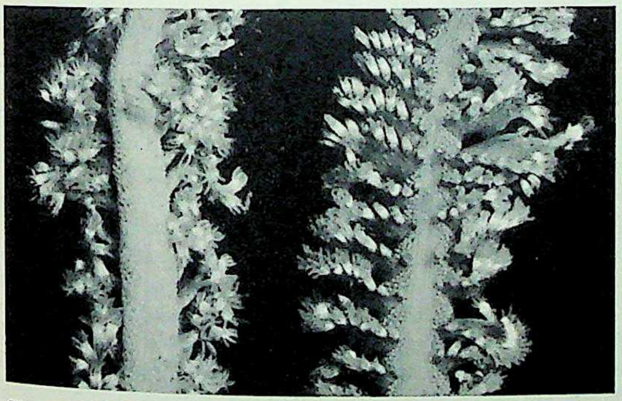


Figure 6 *Portion of sea-pen* Pennatula phosphorea. *The white areas on the polyps are luminous. (× ¾ approx.) (Photograph by Douglas P. Wilson.)*

Figure 7 (above, right) *Section through the light-organ of a deep-sea fish,* Gonostoma elongatum. *The organ lies on the latero-ventral surface of the trunk and is organized so that the light is cast downwards. The photograph is oriented with dorsal aspect above, and exterior (ex) to the right. A pigmented sheath (p.s.) and a reflector (rf) partially envelop a mass of light-generating cells (photocytes, ph). Below, there is a gelatinous body (g.b.) looking like a lens; ep, epidermis or skin; and sc, a scale. (× 252) (Photographs 7 and 8 by A. G. Best.)*

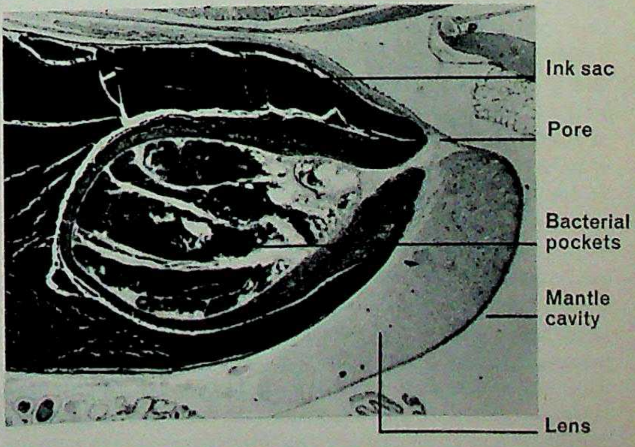


Figure 8 (right) *Section through the bacterial light-organ of a small squid,* Sepiola atlantica. *(× 47)* central nervous system, and the luminous response is a reflex to an external stimulus. Some external stress excites the sense organs of the worm and sensory nerve impulses invade the main nerve cord, from which efferent nerve impulses proceed outwards towards scales in which the luminescent tissue is lodged. A striking feature of the luminescence of scale-worms is that each scale flashes intermittently, and the tiny spots of light blink on and off at a rate of about once per second, many times in succession (figure 3). In the centre of each scale there is a ganglion or node of nerve cells; it appears that repetitive discharge from this is responsible for the succession of flashes. A scale-worm is able to cast off its scales, and when this occurs the scales continue to flash although severed from the body. This continued flashing depends on the activity of the ganglion contained within the scale and does not take place in the absence of the ganglion.

Luminescence in fishes, also, is regulated by the central nervous system. Fishes respond by flashing to tactile stimuli and to pulses of light, and it is probable that many fish flash spontaneously. Unfortunately, most luminous fish are pelagic, very fragile, difficult to capture alive, and short-lived in captivity; consequently, observations of luminescence are very fragmentary. Light-organs of fishes are often arranged in longitudinal series along head and trunk (figure 5). In a North American fish known as the midshipman (*Porichthys*), they light up progressively, like feebly glowing portholes. They are innervated by branches of cranial and spinal nerves and seem to be controlled by the sympathetic nervous system. Nervous impulses proceeding to the light-organs cause the light-generating cells or photocytes to luminesce. Stomiatoid fishes from the ocean depths have, besides serially arranged light-organs, peculiar cheek-organs; these are directly innervated and also possess a rotating mechanism that allows the light-emitting surface to be pulled downwards and concealed [3].

Female glow-worms shine continuously at night, but they can turn their lights on and off at will, and male fireflies flash intermittently. There has long been speculation as to how light-emission is regulated in fireflies, and theories of oxygen-control have received most favour. The photocytes, like other tissues of insects, are aerated by small tracheal tubes, and it was believed that special valves in the tubes could expand or contract so as to allow oxygen to reach the photocytes or to cut it off. This theory has never been satisfactory, because of the difficulty of comprehending how such large masses of tissue could survive without oxygen for very long periods.

It has now been possible to record, from the nerve cord, impulses that precede the flash of light in fireflies (figure 9). The nervous impulses concerned with luminescence always appear in volleys, but it is still not known whether they are proceeding to the photocytes or are directed to the tracheal valves [6]. These observations are of especial interest, because this is the first occasion in which nervous activity connected with luminescence has been determined directly.

Practically nothing is known about the function and manner of light-emission in those squids that contain luminous bacteria. It has been suggested that when pigment in the ink-sac is displaced away from the lenticular surface of the luminescent organ, light can escape to the exterior. In fish with comparable bacterial organs, several control mechanisms are recognized. When light is directed through the abdominal wall, it sometimes waxes and wanes or ceases altogether (for example, in leiognathids and macrourids). These fluctuations seem to be due to concentration or dispersion of pigment in chromatophores—branching pigment cells in the skin. Of two fishes with large bacterial cheek organs, one, *Anomalops*, is able to rotate the organ downwards so as to conceal it; the other, *Photoblepharon*, draws an opaque curtain up over it [4].

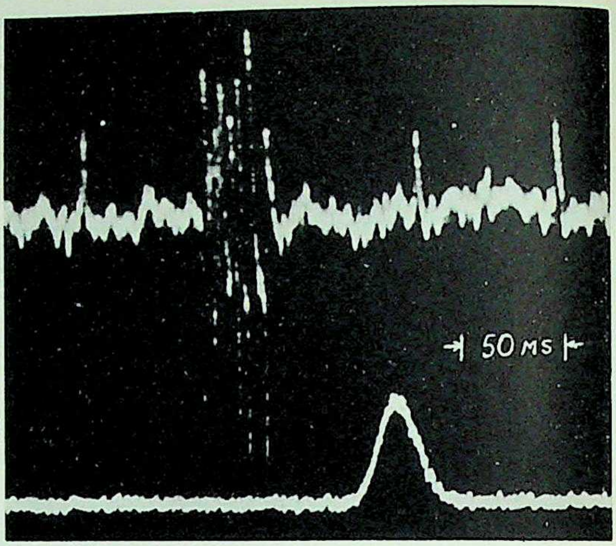


Figure 9 *Recording of nerve potentials from the surface of the lantern of the firefly* Photuris *(upper record), and the subsequent flash (lower record).*

Biochemistry

Light-emitting substances known as luciferins have been obtained in more or less purified form from a wide variety of organisms. An enzyme, luciferase, is usually associated with the luciferin; specifically, it catalyses the oxidation of luciferin, which then emits light [4].

It is now becoming clear that different creatures use very different compounds for light-production. The luciferin of bacteria is an aldehyde-complex of reduced riboflavin-5′-phosphate ($FMNH_2$, dihydroflavin mononucleotide), and bacterial luciferase is a flavin-enzyme. On oxidation $FMNH_2$ is reduced to FMN, and a flash of light is emitted. A mechanism exists for restoring $FMNH_2$ by reduction; this is accomplished by coenzyme I [8]. The luciferin of the piddock *Pholas* (a marine 'clam') also appears to be reduced flavin mononucleotide [2].

Another luminescent system exists in fireflies (Lampyridae). Here the luciferin is 2-(4′-carboxy-thiazole)-6-hydroxybenzothiazole [9]. The luminescent reaction involves the interaction of luciferin and ATP under the catalytic influence of firefly luciferase.

Still another luminescent system exists in *Cypridina*, a minute shelled crustacean allied to water fleas. The luciferin of this animal is a polypeptide linked to a yellow chromophore. *Cypridina* discharges its luminous secretion to the exterior, and the reaction is a very simple one involving only luciferin, luciferase, and oxygen.

The simplest luminescent system so far discovered is that of a jellyfish *Aequorea*. The luciferin is a protein which emits light in the presence of calcium ions.

The weight of evidence at the present time is that luminescence has appeared independently on many occasions, and that various luminescent systems have been exploited.

Colour, spectral composition, and intensity

The luminescences of all animals thus far measured lie in that part of the spectrum visible to man and form rather narrow bands. Usually the relative spectral emission curves have a single peak (figure 10); sometimes, as in the pelagic sea-squirt *Pyrasoma*, there is a smaller peak towards long wavelengths.

Most often the lights are blue or green, especially in marine species, although red lights have been observed on a few occasions (a squid *Thaumatolampas*, and stomiatoid fishes). Firefly lights are more often yellow-green or yellow, and the railroad worm *Phrixothrix* has lights that are green-yellow and red. Relative spectral emission curves for the lights of some twenty species are now available; those of deep-sea animals are especially difficult to determine, but the problems could be resolved by suitable instrumentation [2].

Attempts are now being made to express intensities of bioluminescences in energy units. Some results are given in the table. Luminous secretions fall into the same range of intensities.

Table I

	Intensity (μW/cm² at 1 m)
Single-celled animals:	
Radiolarians	$0{\cdot}06–0{\cdot}05 \times 10^{-9}$
Noctiluca	$0{\cdot}03–0{\cdot}16 \times 10^{-10}$
Sea-pens	$0{\cdot}8–7{\cdot}0 \times 10^{-10}$
Jellyfish, comb-jellies, pyrosomes	Up to $1{\cdot}0 \times 10^{-5}$
Lantern fish *Myctophum*	1×10^{-8}

Experiments suggest that the most sensitive eyes of marine animals can just detect 1×10^{-9} μW/cm² falling upon them. If this is so, then the very brightest flash can just be seen at about 100 m distance in clear oceanic water, and weaker flashes at correspondingly shorter distances [2].

For maximum efficiency, some good correlation should exist between the relative spectral composition of the light of an animal and the relative spectral sensitivity of the eyes of the animal or animals perceiving the light. The two kinds of spectral curves are available in only a few instances. The light of euphausiid shrimps is blue, with maximal emission at 4750 Å; the visual pigment of these animals absorbs maximally at 4620 Å; the efficiency of the light, from the product curve, is 76 per cent (figure 10). Similarly, the light of the lantern fish *Myctophum* possesses maximal energy at 4650 Å, and the visual pigment absorbs most strongly at 4850 Å; the efficiency of the light, estimated from the product curve, is 75 per cent [2]. The lights of pelagic animals are blue or green, and deep-sea animals most often have blue lights. It is in the blue region of the spectrum that active swimmers, such as squids, shrimps, and fish, have greatest visual sensitivity: it is among these animals that we find well-developed eyes. Presumably they are the chief percipients influenced by the feeble sparks of the same or other species.

Many animals in the deeper regions of the ocean, below 500 m or so, are black or red in colour, owing to the presence of melanin, melanoids, carotenoids, ommochromes, and other dark pigments in the skin. The black or brown products absorb evenly through most of the visible spectrum, and the reddish carotenoids and ommochromes absorb in the blue region, where most of the energy of luminescent light lies. The dark liveries of shrimps and fish, for example, reflect very little of the light, whether it be blue residual light of daylight or luminescent light, that falls on them; they have, therefore, protective value by rendering the animals difficult to see [2].

Ecology and behaviour

Animals, as we have seen, produce light in many different ways, and it is highly probable that luminescence has many different roles to play. No satisfactory explanation has yet been offered for the function of luminescence in minute unicellular organisms (protozoans). Sedentary or pelagic coelenterates (sea-pens, jellyfishes), ctenophores (comb-jellies), pyrosomes, and salps (floating sea-squirts) flash only when mechanically agitated or touched; the bright light produced reveals the whole animal and seems to be used for advertising its presence to other free-swimming creatures that encounter it, such as squid and fish. Fireflies and glow-worms, as is well known, use their lights as mating signals, and it is possible that the lights of some fishes are used for the same purpose, since the two sexes sometimes possess dissimilar arrangements of light-organs. When animals, such as euphausiids (small shrimps) and squid, shoal, the lights are a means of keeping the shoal together at night or in the dark ocean depths. Scale-worms seem to throw off their luminous scales as 'sacrifice lures' to distract the attention of aggressors, and the bright luminous clouds produced by deep-sea creatures such as copepods, and shrimp, squid, and fish appear to have a similar function. After discharging their luminous material, these creatures carry out some form of retreat or evasive action, and dart away from the dangerous area. This aspect of luminescence—behaviour and ecology—is the most difficult to study, and much remains to be discovered by students of animal behaviour.

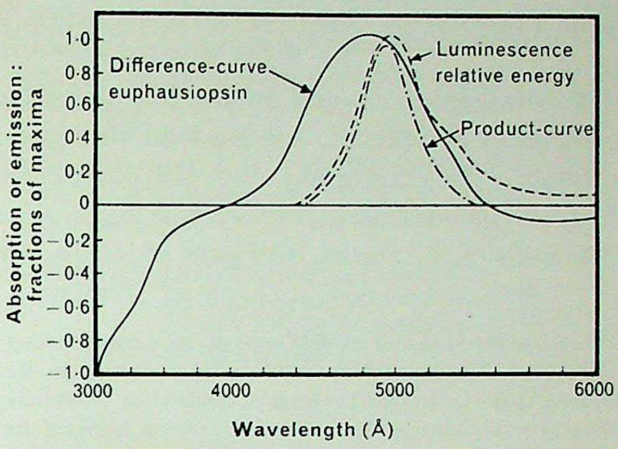


Figure 10 *Light emission and visual pigment in euphausiids (marine shrimps). Curves show a difference curve for the visual pigment of* Euphausia pacifica, *and a product curve for these two variables. The curve for the retinal pigment, illustrating absorption characteristics, was derived from density-differences between bleached and unbleached pigment.*

Acknowledgments

Figure 3 d. From J. W. Hastings and J. Buck, *Biol. Bull., Wood's Hole*, **111**. 105, 1956.

Figure 3 f. From J. J. Chang, *J. cell. comp. Physiol.*, **44**, 371, 1954.

Figure 10. From data of E. M. Kampa and B. P. Boden, *Nature, Lond.*, **175**, 997, 1955; **184**, 1321, 1959.

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Ligand-field theory

L. E. Orgel

The word ligand is used for the ions or molecules that surround the central metal ion in a co-ordination compound. Ligand-field theory deals with the effect that the ligands have on the orbitals of the central ion, and with the stereochemical results of this interaction. The theory has had notable successes, one example being the explanation of the distortion of cupric complexes. The basis of the theory, and some of its applications, are described here by one of the originators.

Ever since the classical work of Werner on the complex salts of metals, the mode of attachment of the co-ordinated groups, the ligands, to the central ion has been an outstanding problem in the theory of valency. The earliest attempt to interpret the co-ordinate link was that of Sidgwick, who envisaged the donation to the central atom or ion of two electrons from each ligand. This idea has since been developed into a more quantitative treatment. Two main approaches have been adopted. The first was the valence bond treatment; the present form of this is largely due to L. Pauling and J. C. Slater. It interprets bonding in terms of the overlapping of the orbitals of the two separate atoms and the pairing of electron spins. This treatment has made a major contribution to chemical theory, particularly in explaining the stereochemistry of complexes in terms of hybrid orbitals. The theory is, however, somewhat inflexible and cannot be used as a basis for the quantitative discussion of some of the interesting physical properties of complexes, such as electronic spectra. The second approach, the molecular-orbital theory, was first developed by F. Hund and R. S. Mulliken. It treats electrons as moving in a potential field produced by the nuclei of all the atoms in a molecule.

The theory that is reviewed in this article is a recent development, based on the electrostatic theory of H. A. Bethe. This regards compounds such as the salts of a hydrated transition-metal ion as an aggregate of ions and molecules that interact with one another, but only electrostatically, and without exchanging electrons. Ligand-field theory generalizes this to incorporate certain features of molecular-orbital theory. It thus gives a more rigid treatment of the effect of the co-ordinating atom in the ligand on the orbitals of the central atom to which it is joined and of the effect this interaction has on the stereochemistry of the complex. It also leads to a more complete understanding of electronic spectra and magnetic properties.

Transition-metal ions

In this article, I shall be concerned with the theory of those properties of metal ions that result from the presence of incomplete shells of *d* electrons. The metals that give rise to ions with partially filled *d* shells are known as transition elements. They constitute the elements from titanium to copper in the first long series of the Periodic Table and the corresponding elements of the two subsequent series (Table 1). The theory which I shall outline applies equally to the chemistry of the rare-earth and actinide elements, which have incomplete *f*-electron shells, but the detailed arguments are more complicated and the consequences are of less chemical interest.

As a preliminary to the development of the theory it is helpful to note some of the ways in which transition-metal ions differ from those of 'typical' metals:

(*a*) Compounds of transition-metal ions with the common anions are usually coloured. The hydrated sulphates of the cobaltous, nickel, and cupric ions, for example, are pink, green, and blue respectively, while the sulphates of the filled-shell ions of zinc and magnesium are colourless.

(*b*) Many transition-metal compounds are strongly paramagnetic; the compounds of the typical elements, with very few exceptions, are diamagnetic.

(*c*) The lattice energies of many binary compounds of typical metals can be understood reasonably well in terms of a purely electrostatic theory. This is not true of the compounds of the transition metals.

(*d*) The stereochemistry of the typical metals is usually consistent with the simplest predictions of ionic theory. The environment of the metal ions is commonly a regular, or almost regular, tetrahedron or octahedron. Some of the transition-metal ions, on the other hand, occur in quite different environments; for example the Pt^{2+} ion occurs in planar complexes and the Cu^{2+} ion in distorted octahedral complexes.

(*e*) Certain transition-metal ions form inert complexes that do not undergo exchange reactions in solution at all rapidly. Thus the Cr^{3+} ion is quite different from the Al^{3+} ion, in that the former undergoes ligand exchange in aqueous solution only very slowly, while the latter reaches equilibrium in aqueous solutions almost instantaneously.

(*f*) There are a number of ligands, for example carbon monoxide and ethylene, that form complexes with transition metals but not with typical metals.

(*g*) The typical metals have one or at the most two stable valencies; the transition metals exhibit a much wider range of valencies—from -1 to 5, for example, in the case of vanadium.

The properties of transition-metal compounds listed above are the most important ones that must be explained by any complete theory of transition-metal chemistry. Ligand-field theory has been rather successful in correlating semi-quantitatively a number of these properties in terms of a very small number of parameters. It has made some direct contribution to the discussion of each of the topics (*a*) to (*f*) listed above; variable-valency of the transition metals is mainly a consequence of the electronic structure of their atoms and depends only indirectly on the type of interaction which we shall discuss. I shall have space to discuss only (*a*), (*b*), and (*d*), which form a rather closely connected group, and I shall have to restrict

Table 1 *The transition elements*

First series	Ti	V	Cr	Mn	Fe	Co	Ni	Cu
Second series	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag
Third series	Hf	Ta	W	Re	Os	Ir	Pt	Au

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the discussion to octahedral complexes. A number of more complete reviews of the subject are available [1–4].

Orbital energies

The foundation of the ligand-field method is to be found in the papers of H. A. Bethe, J. H. Van Vleck, and W. G. Penney and R. Schlapp [5] on the effect of electrostatic fields on the magnetic properties of transition-metal ions. The shapes of the five d orbitals are illustrated in figure 1. It is particularly important to notice that the d_{xy}, d_{xz}, and d_{yz} orbitals have exactly the same shape and exactly the same orientation with respect to the axes in their planes. On the other hand, the $d_{x^2-y^2}$ orbital has the same shape as the d_{xy}, for example, but it is concentrated along the x and y axes rather than between them. The d_{z^2} orbital, like the $d_{x^2-y^2}$ orbital, is concentrated along an axis, but has a different shape. This difference is only apparent, however, for the d_{z^2} can in fact be written as the sum of $d_{z^2-x^2}$ and $d_{y^2-z^2}$ orbitals, each completely equivalent to $d_{x^2-y^2}$ orbitals. Thus the orbitals can be divided into two groups, one with maxima along the axes and the other with maxima between the axes; this division is fundamental to the discussion that follows.

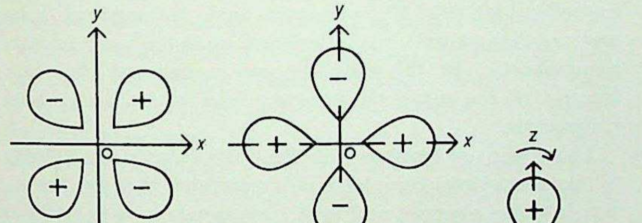

Figure 1 *The five* d *orbitals.*

In an octahedral complex, the effect of the six ligands on the d orbitals of the metal ions may be approximately investigated by considering the effect on the d orbitals of six negative point charges equally spaced along the x, y, and z axes. Similarly six ligands such as water or ammonia can be treated as six point dipoles arranged with their negative ends pointing at the metal. Because the d_{xy}, d_{xz}, and d_{yz} orbitals are tucked away in the gaps between the ligands, while $d_{x^2-y^2}$ and d_{z^2} orbitals point directly at the ligands, the field of the ligands will affect the d_{x^2-y} and the d_{z^2} orbitals, which point along the axes, more than it affects the other orbitals. It is clear from symmetry that the d_{xy}, d_{xz}, and d_{yz} orbitals have the same energy; it is less obvious, but may nonetheless be proved, that the $d_{x^2-y^2}$ and d_{z^2} orbitals also have equal energies. Thus the five d orbitals are no longer of equal energy; the octahedral field of the ligands causes them to split into two groups, one of three orbitals and one of two. The division made on the basis of the orientation of the orbitals has been replaced by one involving a difference in energy. From now on, I shall refer to the d_{xy}, d_{xz}, and d_{yz} orbitals as t_{2g} orbitals and to the others as the e_g orbitals; the letter g is a classifying symbol and has no other significance in the present context.

This splitting of the d orbitals in an octahedral field is shown in the electrostatic energy level diagram (figure 2). In principle Δ, the orbital splitting, can be calculated from the charge on the ligands, the internuclear distance, and the electron distribution in the d orbitals. We shall not consider this aspect of the theory further since we shall see that the electrostatic theory is a crude one and cannot be expected to give an accurate estimate of Δ.

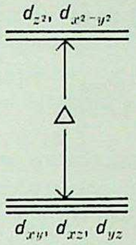

Figure 2 *Energy-level schemes for octahedral co-ordination. The degenerate levels (those of equal energy) are shown slightly separated.*

The next big development in ligand-field theory was the recognition of the importance of covalent bonding and the reformulation of the theory outlined above in terms of the molecular-orbital approach. There are good reasons to believe that the electrons that in a purely electrostatic theory are considered to be isolated on ligands in fact become delocalized to a greater or lesser extent on to the metal, and that those on the metal become delocalized on to the ligands. In the molecular orbital approach we allow for this by combining the orbitals of the ligands with the $3d$, $4s$, and $4p$ orbitals of the metal (or the $(n\text{-}1)d$, ns, and np orbitals in general).

In a regular octahedral complex, the six orbitals of the ligands may be represented as one that is totally symmetric and combines with the $4s$ orbital of the metal; three that have a single node and combine with the p orbitals; and two more that interact with the $3d_{x^2-y^2}$ and $3d_{z^2}$ orbitals—the e_g orbitals (figure 3). The $3d_{xy}$, $3d_{xz}$, and $3d_{yz}$ orbitals do not combine with any of the ligand orbitals and take no part in the bonding.

Whenever a pair of orbitals, one on the ligands and one on the metal, combine together, we get two new orbitals, one

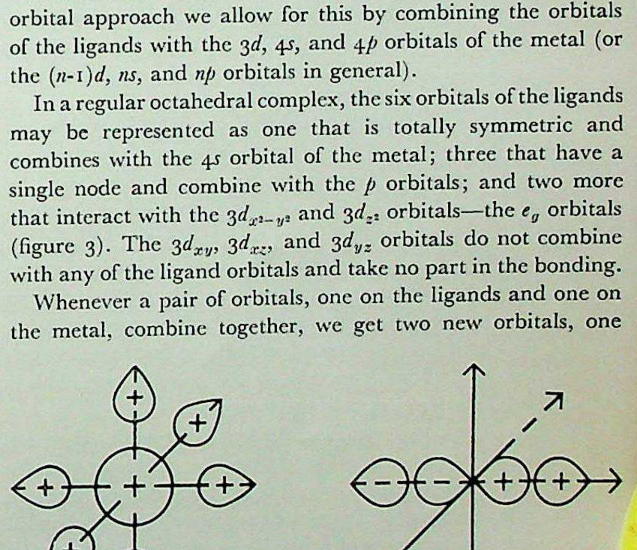

Figure 3 *The σ bonding orbitals of an octahedral complex involving* (a) *the s,* (b) *the* p_x, (p_y *and* p_z) *orbitals,* (c) *the* $3d_{x^2-y^2}$ *orbital,* (d) *the* $3d_{z^2}$ *orbital.*

more and one less stable than either of the original orbitals. Figure 4 shows, in the centre, the new orbital energies formed by the interaction of the metal orbitals, on the left, and those of the ligands, on the right. It is based partly on theoretical considerations and partly on experiment.

Now our complex contains twelve electrons from the ligands and n from the metal ion, n being determined by the nature of the metal and its oxidation state. The former fill the bonding orbitals, leaving just n over to be distributed between the t_{2g} and e_g d orbitals of the complex. That is, we arrive at just the same situation that was predicted in the electrostatic theory; the d shell is split into three stable t_{2g} and two less stable e_g orbitals and these must accommodate as many d electrons as there are on the free ion.

Since both theories predict the same energy-level pattern we cannot use any property that depends only on that pattern to distinguish electrostatic from covalent contributions to the orbital splitting, Δ. The situation is really even more complicated, for it turns out that double bonding also makes a potentially large contribution to Δ. Fortunately, there are a considerable number of interesting aspects of transition-metal chemistry that depend only on the magnitude of Δ and not on its origin. It is with these that we are mainly concerned in ligand-field theory. From now on we shall regard Δ as a parameter that may be determined empirically and that arises from the simultaneous operation of a number of different effects, some electrostatic and some covalent. The breaking down of Δ into individual contributions is a task for the future.

Ions with several *d* electrons

Let us next consider how the d orbitals are filled in octahedral complexes of metal ions with several d electrons. At first sight it would appear that the first six d electrons must go into the t_{2g} orbitals and only when these are filled can electrons begin to enter the less stable e_g orbitals. However, this is not the case, for we have neglected a characteristic quantum-mechanical interaction energy known as the exchange energy, which tends to line up electrons on the same atom with their spins parallel. In fact, for a free ion ($\Delta = 0$) we find that the first five electrons always line up their spins parallel in the ground state. This is one of Hund's rules in atomic spectroscopy.

We have, then, two opposing tendencies at work. They are the ligand-field splitting, which forces the electrons into the t_{2g} orbitals, whenever this is possible, and the exchange effect, which tends to maintain a maximum number of parallel spins. If there are two or three d electrons present, there is no conflict between these two requirements, for the electrons can go into the t_{2g} orbital with their spins parallel. For ions with four electrons, on the other hand, there are two assignments of electrons, each of which is compatible with only one of the above requirements. Either they all go into the t_{2g} orbitals but with one spin opposed to the other three, or three go into the t_{2g} orbital and one into the e_g orbital with all four spins parallel. Which of these arrangements is the more stable depends on the relative magnitude of the ligand-field splitting and the exchange energy, for clearly we have four parallel spins in the free ion when $\Delta = 0$ and only two if Δ is so much larger than the exchange energy that it is dominant in determining the electronic structure. We call these two situations the weak and strong field cases, respectively, for obvious reasons.

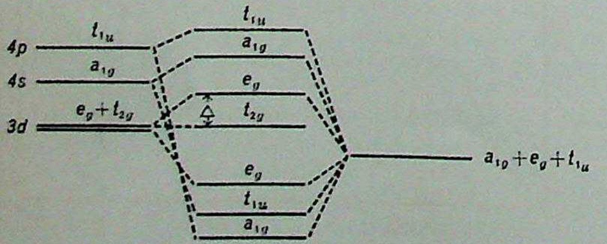

Figure 4 *The molecular-orbital energy-level diagram for an octahedral complex (diagrammatic).*

Ions with five, six, or seven d electrons are like d^4 ions in that they can have either of two electronic arrangements, one of which gives a maximum number of t_{2g} electrons and the other a maximum number of unpaired spins. Once there are eight or more d electrons present, the t_{2g} orbitals are necessarily filled and so there is only one possible d-electron assignment. These relations are illustrated in Table II.

The relative strength of ligand-field splitting and exchange energy in any compound reveal themselves in its magnetic susceptibility. This, for a transition-metal complex, is determined to a large extent by the number of unpaired spins on the metal atom; in fact, the molecular susceptibility k is roughly proportional to $\sqrt{\{n(n+2)\}}$, where n is the number of unpaired spins. It follows that low-field complexes of d^3 to d^7 ions are distinguished from the corresponding high-field complexes by their greater paramagnetic susceptibility. For example, high-field d^6 complexes have no unpaired spins and are diamagnetic, while low-field complexes are strongly paramagnetic. In this way we can understand the main features of the magnetic susceptibilities of transition-metal compounds.

Those who are familiar with Pauling's valence-bond theory of transition-metal complexes will remember that the distinction between covalent and ionic compounds in that theory is often made on the basis of the magnetic criterion for bond type. For ions with four to seven d electrons, this amounts to classifying the complexes with the lower value of the susceptibility as covalent and the rest as ionic. In the above discussion, we arrive at a different explanation of the existence of two classes of complex with different magnetic properties. This explanation does not necessarily depend on the covalent character of the bonds.

Since it is really the spin that is determined experimentally by magnetic-susceptibility measurements, I shall refer to complexes, from now on, as high-spin or low-spin. High-spin is interpreted to mean ionic in Pauling's theory and low-field in ligand-field theory; low-spin corresponds to covalent in Pauling's theory, and high-field in ligand-field theory.

Table II *d electrons in octahedral complexes. n = number of unpaired spins; μ = predicted spin-only moment in Bohr magnetons*

Number of *d* electrons	Arrangement in weak ligand-field		*n*	μ	Arrangement in strong ligand-field		*n*	μ
	t	*e*			*t*	*e*		
1	↑	—	1	1·73	↑	—	1	1·73
2	↑ ↑	—	2	2·83	↑ ↑	—	2	2·83
3	↑ ↑ ↑	—	3	3·87	↑ ↑ ↑	—	3	3·87
4	↑ ↑ ↑	↑	4	4·90	⇅ ↑ ↑	—	2	2·83
5	↑ ↑ ↑	↑ ↑	5	5·92	⇅ ⇅ ↑	—	1	1·73
6	⇅ ↑ ↑	↑ ↑	4	4·90	⇅ ⇅ ⇅	—	0	0
7	⇅ ⇅ ↑	↑ ↑	3	3·87	⇅ ⇅ ⇅	↑	1	1·73
8	⇅ ⇅ ⇅	↑ ↑	2	2·83	⇅ ⇅ ⇅	↑ ↑	2	2·83
9	⇅ ⇅ ⇅	⇅ ↑	1	1·73	⇅ ⇅ ⇅	⇅ ↑	1	1·73

Spectra and Δ values

In order to produce a quantitative theory, it is necessary to determine Δ, the ligand-field splitting. This is usually achieved by detailed interpretation of the visible spectrum of the complex ion in question. Let us consider first the case of an octahedral complex of a metal ion with just one d electron. Then it is quite clear that in the ground state (the state of lowest energy) of the complex, this electron occupies one of the t_{2g} orbitals. In the course of the electronic transitions that are responsible for the visible (and near infra-red and near ultraviolet) spectra of molecules, electrons are transferred from one orbital to another. In our d^1 complex, only one transition within the d shell is possible, the one that transfers an electron from the t_{2g} orbital to the less stable e_g orbital. Thus, if we can identify this transition, we can determine at once the energy separation Δ.

In figure 5 the spectrum of the $[Ti(H_2O)_6]^{3+}$ ion is reproduced. There is just one transition in the visible region, at about 5000 Å, corresponding to an energy of about 20 000 cm⁻¹ or 60 kcal. This transition has now been identified as the $t_{2g} \rightarrow e_g$ transition and so may be used to fix Δ for the $[Ti(H_2O)_6]^{3+}$ ion at about 60 kcals.

The analysis of the spectra of ions with more than one d electron is much more difficult, but the identification of the absorption bands has been achieved in a way that leaves no reasonable doubt about the assignments. The essential difficulty is that the different d electrons interact strongly with each other, so that transitions do not always involve the simple transfer of one electron from the t_{2g} to the e_g orbitals. It is then necessary to compute the complete energy-level diagram for the ion as a function of the energy, Δ, of the ligand field. In figure 6 this is done for the most interesting states of the Mn^{2+} ion.

The ground state for this ion is ^6S, which is taken, for this diagram, to have zero energy. The excited states are ^4G, ^4P, ^4D, ^4F. The energy of these states is obtained from atomic spectra. The diagram shows the splitting of these levels as the energy of the ligand field increases. The state on the left-hand side is for Δ = 0.

The ground state has all the five spins parallel; its configuration is necessarily $(t_{2g})^3\ (e_g)^2$. It will be unaffected by the ligand field. The excited states are usually split into a number of states by the ligand field, just as the single d electron state of an atom with one d electron is split into a t_{2g} and an e_g state. In general, lines that slope down from left to right in figure 6 correspond to states in which there are four electrons in the t_{2g} orbital. Similarly, horizontal lines correspond to $(t_{2g})^3(e_g)^2$ states and upward sloping lines to $(t_{2g})^2(e_g)^3$ states.

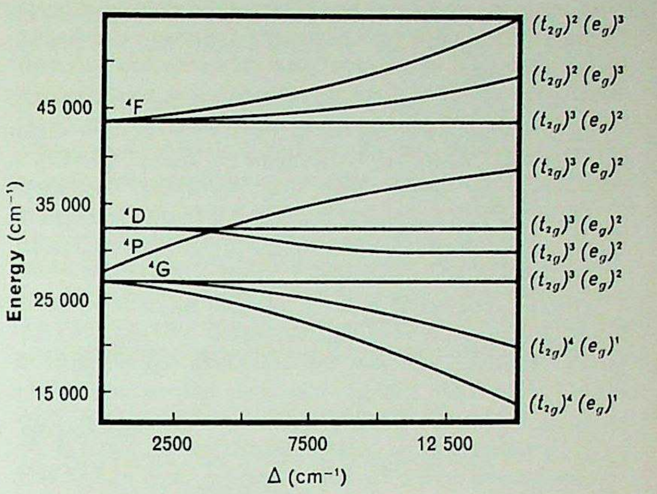

Figure 6 *Energy-level diagram for a* d⁵ *ion,* Mn^{2+}.

The spectrum of the $[Mn(H_2O)_6]^{6+}$ ion is illustrated in figure 7. We should have a satisfactory account of this spectrum if we could find a value of Δ such that the vertical distances between the energy zero (the ground state) in figure 6 and the successive upper lines corresponded accurately to the energies of the successive observed transitions. This can, in fact, be achieved at least semi-quantitatively if we suppose that Δ = 7800 cm⁻¹ (1 eV = 8068 cm⁻¹).

There is a very large literature concerned with the identification of the $d \rightarrow d$ transitions in metal complexes, and hence with the determination of Δ. The colours of transition-metal complexes can now be understood fairly completely along these lines. The problem of intensities has also attracted much attention. In this article I have necessarily oversimplified the discussion of spectra and have neglected many important details in order to illustrate the way in which the main parameter of the theory, the orbital separation, Δ, is determined. Some of the most reliable Δ values found in this way are shown in Table III. For a more detailed discussion the reader is referred particularly to the review article by D. S. McClure [6].

Table III reveals a number of important regularities:

1. Δ values for the same ligand with metal ions in different valencies increase very rapidly with the valency. Thus Δ values for hydrates of divalent metals of the first series cluster about 10 000 cm⁻¹, while those for trivalent ions are about twice as large.

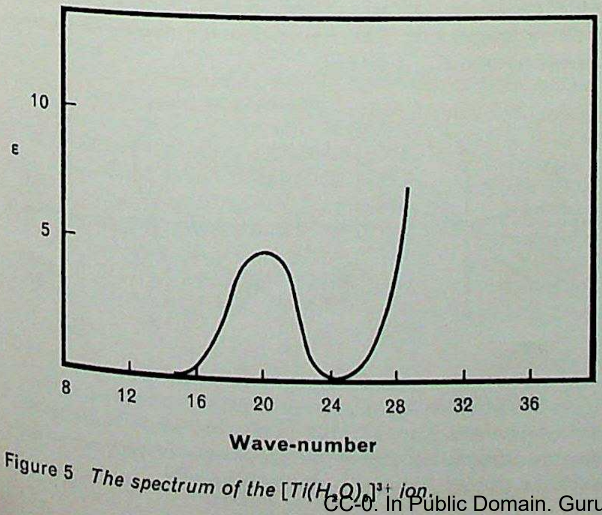

Figure 5 *The spectrum of the* $[Ti(H_2O)_6]^{3+}$ *ion.*

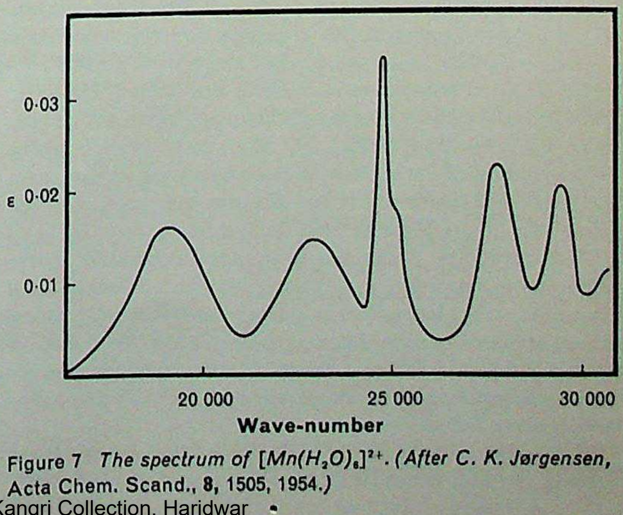

Figure 7 *The spectrum of* $[Mn(H_2O)_6]^{2+}$. *(After C. K. Jørgensen,* Acta Chem. Scand., **8**, 1505, 1954.*)*

2. Δ values for a given ligand and corresponding elements of different transition series increase rapidly from the first to the later series.
3. Ligands can be placed in an order such that Δ increases along the series for any metal ion (with a very few slight exceptions). This series is essentially the same as Tsuchida's spectroscopic series, which was discovered empirically before the development of the ligand-field interpretation of the spectra. In Table III the ligands are given in their order in the spectrochemical series.

With this information about Δ available we can now return to a discussion of the transition from high-spin to low-spin complexes. We have seen that this transition depends upon Δ achieving a certain critical value and thus overcoming the exchange interaction. Clearly, the complexes are more likely to be low-spin if they contain ligands to the right of the spectrochemical series. For each metal ion, there should be a point in the spectrochemical series such that complexes formed by ligands to the left of it are of the high-spin type and those formed by ligands to the right are of the low-spin type. In general this is what is observed; for example the Fe^{2+} ion forms low-spin complexes with phenanthroline and the cyanide ion, but high-spin complexes with ions to the left of phenanthroline in the series.

Next, we may compare the complexes of different metal ions with the same ligand. If we choose metal ions from the same column of the Periodic Table, say nickel, palladium, and platinum, or iron, ruthenium, and osmium then, since Δ increases with atomic weight, the compounds of the heavier elements should form low-spin complexes more readily. This conclusion is strengthened when it is realized that the exchange forces resisting spin-pairing become weaker in the heavier metals. In this way we may understand the rarity of high-spin complexes among the compounds formed by the heavier elements.

If we consider the successive elements in a given transition series it turns out that the resistance to spin-pairing is very strongly dependent on the number of d electrons present. Calculation shows, for example, that a much larger value of Δ is required to bring about spin-pairing in d^5 ions than in d^6. This is why the complexes of Co^{3+} are almost all low-spin while those of Fe^{3+} are in most cases high-spin. The detailed quantum-mechanical theory gives a very reasonable account of the distribution of high-spin and low-spin complexes.

Stereochemistry of the Cu^{2+} ion

The Cu^{2+} ion has nine d electrons and these, in a regular octahedral complex, must adopt the electron configuration $(t_{2g})^6(e_g)^3$. If we consider the electronic structure more fully we notice that the $(t_{2g})^6$ sub-shell of electrons is a filled sub-shell and so its occupation is uniquely determined. However, the $(e_g)^3$ sub-shell admits of two different arrangements, namely $(d_{z^2})^2(d_{x^2-y^2})^1$ and $(d_{z^2})^1(d_{x^2-y^2})^2$. Since the d^{10} shell is spherically symmetrical, these two arrangements correspond to a spherical shell from which an electron has been removed either from the xy plane or from the z axis.

The internuclear distance in a complex is determined by the requirement that the attractive force between the nucleus and the negative ion just balances the repulsive force due to the interpenetration of their electron clouds. Clearly, this repulsive force is different in different directions if the metal ion does not have spherical symmetry, and so the equilibrium internuclear distances are not all the same.

Table III *Values of ligand-field splitting Δ. Values for* d^4 *and* d^9 *systems are only approximate (italics indicate low-spin complex)*
(From C. K. Jørgensen's thesis, Copenhagen, 1957)

	$6Br^-$	$6Cl^-$	$6H_2O$	$6NH_3$	$3C_2H_4(NH_2)_2$	$6CN^-$
3 d^1						
Titanium (III)	—	—	20 300	—	—	—
3 d^2						
Vanadium (III)	—	—	17 700	—	—	—
3 d^3						
Vanadium (II)	—	—	12 600	—	—	—
Chromium (III)	—	13 600	17 400	21 600	21 900	26 300
4 d^3						
Molybdenum (III)	—	19 200	—	—	—	—
3 d^4						
Chromium (II)	—	—	13 900	—	—	—
Manganese (III)	—	—	21 000	—	—	—
3 d^5						
Manganese (II)	—	—	7 800	—	9 100	—
Iron (III)	—	—	13 700	—	—	—
3 d^6						
Iron (II)	—	—	10 400	—	—	*33 000*
Cobalt (III)	—	—	*18 600*	*23 000*	*23 300*	*34 000*
4 d^6						
Rhodium (III)	*18 900*	*20 300*	*27 000*	*33 900*	*34 400*	—
5 d^6						
Iridium (III)	*23 100*	*24 900*	—	—	*41 200*	—
Platinum (IV)	*24 000*	*29 000*	—	—	—	—
3 d^7						
Cobalt (II)	—	—	9 300	10 100	11 000	—
3 d^8						
Nickel (II)	7 000	7 300	8 500	10 800	11 600	—
3 d^9						
Copper (II)	—	—	12 600	15 100	16 400	—

The situation for a d^9 ion is illustrated in figure 8. If the missing electron comes from the $d_{x^2-y^2}$ orbital (figure 8a), the repulsions are weaker along the x and y axes than along the z axis and so we should expect four short bonds in the xy plane and two longer ones along the z axis; the arrows represent the unequal attractions. On the other hand, if the electron is missing from the d_{z^2} orbital (figure 8b) it is the two bonds along the z axis that should be shorter than the other four.

In either case, the d^9 ions should not occur in regular octahedral environments. The theoretical calculation of the exact distortion to be expected is much more difficult and is still a somewhat controversial problem. The experimental evidence, however, is quite clear; in all but one or two of the many cupric complexes which have been studied, there are four short and two long bonds. This shows that the missing d electron comes from the $d_{x^2-y^2}$ orbital.

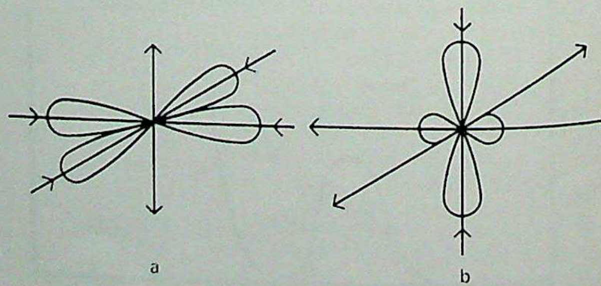

Figure 8 *Distortion due to absence of* (a) $d_{x^2-y^2}$ *or* (b) d_{z^2} *electron from the closed* d^{10} *shell. In* (a), *the ligands in the xy-plane are attracted because of the less shielded nuclear attraction; in* (b), *the ligands along the z-axis are attracted.*

Arguments exactly like those for the Cu^{2+} ion apply to d^4 ions, since these have the electron configuration $(t_{2g})^3(e_g)^1$, again with an unbalanced e_g electron. It is found that, just like the Cu^{2+} ion, the Cr^{2+} ion, and Mn^{3+} ions almost always occur in environments with four near neighbours in a plane and two more distant ones completing a distorted octahedron. Particularly convincing are the structures of the difluorides, MF_2, of the transition metals. The compounds of Mn^{2+}, Fe^{2+}, Co^{2+}, Ni^{2+}, and Zn^{2+} all have the rutile structure, with almost regular octahedral co-ordination, while the Cr^{2+} and Cu^{2+} compounds have a closely related structure but with distorted environment about the metal. It is difficult to think of any explanation except the one given above of the very different behaviour of just these elements in a transition series.

The case of the Cu^{2+} ion is particularly interesting because it is one of the few places where Pauling's valence-bond method and ligand-field theory lead to sharply divergent conclusions. According to Pauling, the Cu^{2+} ion in its planar complexes has the configuration $(3d)^8(4p)^1$ and forms four covalent bonds. According to ligand-field theory the planar complexes are just strongly distorted $(3d)^9$ complexes. Experiment shows unambiguously that the latter interpretation is correct.

This article may have given the impression that ligand-field theory contradicts the usual valence-bond interpretation of transition-metal chemistry. This is not really the case. There are a few points on which there is sharp disagreement between the two theories, but these are not crucial. The valence-bond method could well be adapted to rationalize the new information that has accumulated in the past decade or so.

The major difference between the two theories is that the valence-bond method is qualitative; for example, no one has yet seen how to use it to make detailed calculations of optical or magnetic properties. The ligand-field method, in the author's opinion, is no more difficult to understand, explains qualitatively as wide or even a wider range of phenomena, and also provides the basis for really detailed calculations of molecular properties. Ideally, all chemists should be familiar with both theories.

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Book reviews

COMPUTERS

Mathematical Programming, *by S. Vajda. Pp. ix+310. Addison-Wesley Publishing Co. Inc., Reading, Mass. and London. 1961. 68s. net.*

This comprehensive book, on a key subject in operations research, begins with mathematical preliminaries, such as inequalities, algebra of duality, graphs, and combinatorial theory. Methods of linear programming are then explained, including the usual special techniques for transportation and assignment.

Applications are then discussed. There is a chapter on discrete programming where integral solutions only are allowable. In recent years the subject has been extended in two directions, firstly to the case where some stochastic elements are introduced into the model, secondly to macroscopic problems, where there is a need for non-linear programming. Both these cases are treated in separate chapters. Finally, there is a short chapter on dynamic programming.

In the text there are a number of worked examples, and solutions are given to the exercises. There is also an adequate bibliography. The book will be very suitable as a text for students of operational research and applied mathematics generally. It will also be of interest to industrialists seeking to know what programming can do for them.

L. S. Goddard

Linear Programming, *by G. Hadley. Pp. xii+520. Addison-Wesley Publishing Co. Inc., Reading, Mass. and London. 1962. 74s. net.*

Linear programming is the mathematical technique that is used to solve the problems that arise in the practical application of operations research.

Two excellent elementary introductions to linear programming have already been produced: Vajda's 'Theory of games and Linear Programming' and the very amusing 'Compleat Strategyst' by Williams. Both of these are not only somewhat dated but concern themselves more with results than with methods, and up to now a really good, but still comprehensible, book on techniques has been lacking.

Hadley's new book fills this gap with distinction. Not only is it written from an elementary standpoint, but it provides a résumé of the relevant basic mathematics. From this point there is a step-by-step account of most of the methods available in the field. Thus, after discussing the simplex algorithm of Dantzig and analysing its computational deficiencies, the book goes on to describe the two-phase variant of the method and then of the revised simplex method and duality.

Numerous applications are used to illustrate the text, and engineering production, oil refinery operation, and the organization of transportation systems all receive detailed consideration.

The book ends with a basic analysis of the 'firm' which should interest top management.

There is no doubt that Hadley's book is a timely one, and it can be thoroughly recommended.

A. D. Booth

ASTRONOMY

Explanatory Supplement to the Astronomical Ephemeris and The American Ephemeris and Nautical Almanac, *prepared jointly by the Nautical Almanac Offices of the United Kingdom and the United States of America. Pp. xii+505. H.M. Stationery Office, London. 1962. 42s. net.*

This book is of wider scope and of far greater importance than its title suggests. Conceived nearly twenty years ago, in H.M. Nautical Almanac Office, as a replacement for the rather lengthy explanation that had appeared in the Nautical Almanac from 1931 to 1942, the supplement gradually grew into a book. Its publication was wisely delayed until after the fundamental changes in the almanacs brought about by the introduction of ephemeris time in 1960, which year also marked the unification of the American and British almanacs. This unification led naturally to the sharing of preparation of the supplement between the two Nautical Almanac Offices so that the combined experience of both could be fully utilized. Competent editorship has ensured that a script with many authors has been transformed into a pleasingly integrated volume.

A full, clear, and rigorous explanation of the derivation and use of the contents of the current almanacs is given and also a guide to the contents of previous almanacs right back to the first one issued, that for 1767. The book does more than this, however. Some of the eighteen sections into which it is divided are comprehensive treatments of topics in positional and dynamical astronomy and in chronology, containing much material that is not easily accessible elsewhere, and certainly not in so convenient or so authoritative a form. Other sections are compilations of useful data such as that in which computing techniques of special relevance to astronomical calculations are gathered together. In short, this is a reference book that no working astronomer or serious astronomical student can afford to be without. *R. H. Stoy*

NUCLEAR PHYSICS

Elementary Particles, a Short History of some Discoveries in Atomic Physics, *by Chen Ning Yang. Pp. 70. Princeton University Press; Oxford University Press; London. 1962. 22s. net.*

This is a delightful introductory volume on elementary particles. Professor Yang describes the discovery of the particles and the development of this exciting branch of physics in a language which most laymen would understand. The great point about the book is that, in addition to giving the facts, it affords an insight into the thinking and working of the minds of those gifted men who have created the subject; to this class Professor Yang himself belongs. He is no doubt one of the most vital physicists alive today. Thus I have read the book as an introduction to his own processes of thought, and from this, amongst other virtues, the book derives its value. Professor Yang has profusely quoted from J. J. Thomson, Einstein, C. T. R. Wilson, and others. Perhaps the last quotation in the book from Einstein is worth repeating: 'Can we ever hope to find the right way? I answer without hesitation that there is, in my opinion, a right way and that we are capable of finding it.' Yang ends his book by adding: 'The faith so movingly expressed by Einstein still sustains the physicists today.' *A. Salam*

NUCLEAR MAGNETIC RELAXATION

Nuclear Magnetic Relaxation, *by N. Bloembergen. Pp. ix+178. W. A. Benjamin Inc., New York. 1962. $3.95.*

This book is the first in a new paper-backed series entitled 'Frontiers in Physics'. The books will consist of lecture notes and collections of reprints, with introductory or explanatory notes by the authors.

One might be excused for flinching at what seems to amount to another review periodical, but it is certainly difficult to imagine a more valuable first volume. The book consists of photographic reproductions of Professor Bloembergen's University of Leiden thesis (1948) and one research paper on the interaction of nuclear spins in a crystalline lattice.

Anyone who seeks to understand magnetic resonance phenomena must be familiar with the classic paper by Bloembergen, Purcell, and Pound (*Phys. Rev.*, 73, 679, 1948) dealing with nuclear spin relaxations induced by dipolar interactions in solution. Those who have considered it a necessary part of their education to work through this paper would have found the way made a great deal easier by this book. It contains essential background material which is often difficult to find elsewhere, and concludes with six pages of notes by the author, drawing attention to errors and important subsequent developments.

Very few doctorate theses are worthy of publication at the time of their writing. A thesis which can justifiably be published fourteen years after its completion is clearly something out of the ordinary. *A. Carrington*

REACTION MECHANICS

Theory of Molecular Excitons, *by A. S. Davydov (translated from the first Russian edition by M. Kasha and M. Oppenheimer, Jr.). Pp. ix+174. McGraw Hill Book Co. Inc., New York and London. 1962. 62s. net.*

We now have good evidence for the existence of 'excitons' in ionic solids, and in semiconductors such as CdS and Ge. The theories developed by Frenkel, Peierls, Mott, and Wannier in the 1930's have now been greatly extended, and there is the beautiful experimental work on the optical absorption spectra of thin crystals by Gross, Nikitine, and others which has given information on exciton structure. In the case of molecular crystals, in particular for aromatic compounds such as naphthalene, anthracene, and phthalocyanine, where we are concerned with π-electrons, the optical absorption spectra, photoconductivity, and the mechanism of energy transfer in the solid are usually interpreted on the basis of Davydov's exciton (free and localized) theory. This theory was developed in 1948 for solids in which there is weak interaction between neighbouring molecules. Davydov's book was written in 1951 and became something of a classic. It has now been translated by Professor Kasha, who has himself made important contributions in this field, and by Professor Oppenheimer. Minor corrections have been made, and the appendices list recent papers by Davydov and others on topics such as excitons in molecular crystals; absorption spectra in the ultra-violet, visible, and infra-red; and luminescence. This is an outstanding book and deserves to be widely read. There have been a number of reviews since this book was written, but the subject-matter still remains of considerable interest to scientists working in solid-state physics and chemistry. *A. D. Yoffe*

NUCLEAR PHYSICS

Particle Accelerators, *by M. S. Livingston and J. P. Blewett. Pp. xvi+666. McGraw Hill Book Co. Inc., New York and London. 1962. £6 1s. 6d. net.*

This excellent book is a first-hand account of the rapid and exciting development, both scientific and technical, in the short history of these basic instruments of nuclear physics. The authors have each played a leading part in the development of particle accelerators.

The various types of accelerator are discussed in separate chapters, commencing with one on the earliest low-voltage generators, and concluding with one on the principle of alternating gradient focusing and the astonishing machines that arise from this principle. The order is mainly chronological, this being of course also an order of increasing complexity, but the importance of general principles and common techniques is stressed as they arise. Chapters of general interest and value are interposed between the others, and concern ion sources, magnets, the motion of particles in fields, phase stability, and shielding. The first three help to establish the basic background on which the art is based. The sophisticated principles of phase stability and strong focusing are explained and derived mathematically in a general way, and then applied to the specific cases of interest. The chapter on shielding is especially appropriate at a time when many of the new accelerators under construction or design are intended to provide beams much more intense than those at present available.

The contents are well arranged, and explanations are supplemented by the many useful diagrams. References at the end of each chapter form valuable lists, mainly of papers of classic original content or specific technical value. The book will be of value to workers in the accelerator field and of interest to physicists in general. It should be read by the younger scientists now using the various accelerators that it describes. *L. Riddiford*

ELECTRON MICROSCOPY

Traité de microscopie électronique, *edited by C. Magnan. Part I, pp. viii+650; Part II, pp. viii+651–1301. Hermann, Paris. 1961. 300 NF.*

This monumental work contains a complete account of the theory and practice of electron microscopy, written by a team of French scientists, all of whom have done important original work in the subject. In volume I the basic theory of the instrument and the practical details of commercial models are described by C. Magnan, and the methods of electron microscopy of solid surfaces and phenomena of electron interference and diffraction by C. Fert. Agnes Oberlin and C. Tchoubar contribute chapters, some jointly and some individually, on the theory and practice of electron diffraction, on specimen preparation, on crystallographic and morphological applications, and on the study of transformations and other dynamic processes by cinematographic methods.

Volume II is devoted to accounts of the special methods of specimen preparation, and to typical results obtained in the most important fields of application of electron microscopy. A. Saulnier deals with metallurgy and metal physics. Nina Carasso and P. Favard give the preparative methods of biological material in one chapter, and a survey of the new discoveries made about its ultrastructure in the next chapter; the pair are two of the longest chapters in the book. The last chapter, by P. Favard, Nina Carasso, and Agnes Oberlin, is devoted to biocrystallography, by which is meant the study of biological macromolecules and the ways in which they form various types of regular array, including true crystals.

The treatise is planned and written with Gallic clarity and comprehensiveness. Not only is the literature of the whole world drawn upon, each chapter ending with a very full bibliography, but the authors have gone to great trouble to collect the most illuminating micrographs from laboratories in many countries. 'Anglo-Saxon' authors (in the phrase frequently used in the text) are very well represented, though perhaps less than justice has been done to some of the German work. As would be expected for the price, the production of the two volumes is of the highest class. In particular, 33 of the best micrographs are reproduced by a new process on what appears to be photographic paper, and these plates are inserted at the appropriate places in the text. Altogether it is a magnificent production, which is bound to stand as the definitive work on electron microscopy for many years to come.

V. E. Cosslett

Techniques for Electron Microscopy, *edited by D. Kay. Pp. xvii+331. Blackwell Scientific Publications, Oxford. 1961. 63s. net.*

Advances in electron microscopy have been so rapid that it is difficult for most workers to keep in touch with new methods. The appearance of an authoritative and up to date book of this sort is greatly to be welcomed. So far as the reviewer is aware, no other book in English covers such a wide range. The various chapters deal with the operation of the microscope, ancillary apparatus, specimen-support films, techniques for mounting, dispersing, and disintegrating, replica and shadowing methods, optical selection of specimens, examination of small particles, fixation, embedding and staining, thin sections, preparation of metals and crystals, metal films, electron diffraction, and reflection electron-microscopy. Each chapter is written by an expert in the field. The treatment is fairly comprehensive, and excellent bibliographies are provided. It is inevitable that the personal preferences of the authors come to the fore occasionally, but on the whole the book gives a well-balanced account of modern methods. If it can be kept up to date by frequent revision it is assured of a permanent place in the literature of electron microscopy. *R. Barer*

CHEMICAL DICTIONARY

The Condensed Chemical Dictionary *(sixth edition), edited by A. and E. Rose. Pp. xix+1257. Reinhold Publishing Corporation, New York; Chapman and Hall Ltd, London. 1961. £7 net.*

The new edition of this well-known dictionary appears in a slightly larger format and with some fifty additional pages. It has been considerably revised, some obsolete information having been deleted and a great deal of new material inserted. This is spread over many fields, such as polymers, plastics, organometallic chemistry, nuclear chemistry, and fuels, to mention only a few. The entries on specific compounds are unchanged in type and include information on properties, sources, uses, and shipping regulations. Concise definitions are also given for a wide range of chemical terms. Trade names also figure prominently among the entries, though these, not unnaturally, refer in the main to products in current use in the United States. The high standard of the earlier editions is fully maintained, and the book remains an excellent practical reference work both for chemists and for the many others who require concise and accurate information on chemical names and terms.

H. J. Emeléus

CHEMICAL ANALYSIS

Chemical Analysis – The Working Tools, *edited by C. R. N. Strouts, H. N. Wilson, and R. T. Parry-Jones, with the assistance of J. H. Gilfillan. Vol. I, pp. xvi+467; vol. II, pp. x+479; vol. III, pp. vii+273. Oxford University Press Ltd, London. 1962. £7 7s. net the set.*

These three volumes describe the general analytical methods used by Imperial Chemical Industries Limited. The first deals with fundamental aspects and procedures of analytical chemistry. Starting from considerations of accuracy, statistical methods, and sampling, it proceeds through discussions of basic equipment to problems of weighing and the determination of temperature, pressure, density, and specific gravity. The calibration of volumetric glassware and the preparation of standard solutions is most authoritatively treated. An important new chapter deals with titrations in non-aqueous solvents, and other topics include the determination of gases in metals by vacuum fusion, fractional distillation, the determination of melting points, and chromatography in all its aspects.

The second volume concentrates on physical methods of analysis, such as pH determinations, electrometric titrations, conductimetry, polarography, electro-deposition, and every aspect of emission and absorption spectrophotometry. The chapters on X-ray diffraction and X-ray fluorescence spectrometry should be of particular value.

The last volume is devoted to the analysis of organic compounds above the ultramicro level and to the determination of molecular weights. A surprising omission was the failure to refer to the oxygen flask method.

This work is well documented, and there are individual indexes to each volume. It bears the stamp of authority and is packed with information derived from wide experience. *H. I. Irving*

ORGANIC CHEMISTRY

Advanced Organic Chemistry, *by Louis F. Fieser and Mary Fieser. Pp. ix+1158. Reinhold Publishing Corporation, New York; Chapman and Hall Ltd, London, 1962. £5 12s. net.*

The question most likely to be asked about this book is, how does it differ from the third edition of Fieser and Fieser's 'Organic Chemistry'? The simple answer is that it is essentially a drastically revised edition. It develops the subject from the beginning and is 'advanced' only in that it covers a wide field of organic chemistry and refers very frequently to recent literature. The claim is made that it provides a complete account of fundamental organic chemistry. It does not deal, however, with heterocyclic chemistry, mentioning in passing only a few heterocyclic compounds such as uric acid. Further, for many special fields which are said to be less active (including alkaloids!), readers are referred to 'Organic Chemistry'.

Any reviewer will find some features about the book with which he will disagree. One may be mentioned here. Surely it is time that D-tartaric acid was given the correct L configuration by the Fiesers. It is illogical to say (p. 946) that D-threose gives L-tartaric acid on oxidation. *T. G. Halsall*

Hydroboration, *by Herbert C. Brown. Pp. xiii+290. W. A. Benjamin Inc. New York. 1962. $10.*

A 'hydroboration' is a reaction in which a boron-hydrogen linkage adds on to a multiple bond between carbon and carbon, nitrogen, or oxygen. Since 1956, when the author of this book and his collaborator B. C. Subba Rao first recognized the occurrence of such a reaction with ethyl oleate, hydroboration has become one of the main synthetic tools of the organic chemist. In the first place, it provides a new route, more versatile and convenient than any other, to the organoboranes, compounds of much interest in themselves. Secondly, these organoboranes can be subjected to various simple chemical treatments which eliminate boron and give hydrocarbons, alcohols, and so on, not readily obtainable in other ways; here lies the present focus of interest in hydroboration. Syntheses of this kind form the subject-matter of a flood of recent publications. Thirdly, the organoboranes have possibilities, so far barely glimpsed, as synthetic agents for organometallic compounds, and it is certainly conceivable that they might soon become a useful alternative to the traditional Grignard reagents for this purpose.

The same skill which guided the spectacular development of hydroboration in the author's own laboratory at Purdue University is manifest in the writing of this excellent book. It gives a clear, well-organized and easily read account of all the main methods and applications of hydroboration, without excessive factual detail but with an adequate number of references. It is sure to become the main first source of information on hydroboration in all research laboratories concerned with organic or organometallic synthesis. *H. G. Heal*

CRYSTALLOGRAPHY

Diffuse X-ray Reflections from Crystals, *by W. A. Wooster. Pp. xii+200. Clarendon Press; Oxford University Press, London. 1962. 35s. net.*

According to the dust cover, this is the first book in which a unified treatment of all the various aspects of diffuse reflections has been attempted. This may not be literally true, but it is perhaps the first in which the subject has been presented with an emphasis on the observable phenomena and the experimental methods. After an introductory general treatment of diffraction by a sinusoidally perturbed lattice and a description of the apparatus required, the main topics discussed are the determination of elastic constants and vibration spectra of crystals from the thermal diffuse scattering; scattering due to structural imperfections; and diffuse scattering from molecular crystals. As might be expected from the author's research interests, the space devoted to the three types of scattering is divided in the approximate ratio 3 : 2 : 1. In simple structures thermal scattering and scattering due to imperfections are well accounted for by theory, but the often very beautiful diffuse patterns given by molecular organic crystals cannot be explained in full detail.

The level is such that the book would be intelligible to honours students, though it is difficult to imagine their having leisure to digest it. It can be warmly recommended to research students, for whom the wealth of references is a particularly valuable feature.

A. J. C. Wilson

CANCER RESEARCH

Advances in Cancer Research, *Vol. 6, edited by Alexander Haddow and Sidney Weinhouse. Pp. x+524. Academic Press Inc., New York and London. 1962. 86s. net.*

It has been the editorial policy of 'Advances in Cancer Research', since the first volume appeared in 1953, to provide a selected number of critical reviews—some six to eight per volume—by recognized authorities in their respective fields. The fact that emphasis is put on the critical assessment of results and interpretations, rather than on the mere documentation and sifting of published data, makes the series particularly valuable, even at a time when scientific reviews are plentiful. The previous five volumes have served as a useful standby for investigators in cancer research. The latest number maintains the same high standards.

Of the eight reviews in this volume, two deal with leukaemia, three with biochemical aspects of cancer, and one each with plant tumours, radiation chimeras, and cancer chemotherapy.

Of the two on leukaemia, one is by L. Gross, on the viral aetiology of the disease in mice, which covers, in condensed form, about the same ground as chapters seven to nine of his book on oncogenic viruses; the other is by Miller, on the aetiology and pathogenesis of the disease—an excellent review breaking new ground, to be recommended to all those working in the field. The review on plant tumours by Braun and Wood is timely, and should serve as a stimulus for further work in this largely neglected field. The three biochemical reviews are by Bodansky, on blood enzymes in cancer and other diseases; by Timmis, on antagonists of purine and pyrimidine metabolites and of folic acid; and by Weber, on the behaviour of liver enzymes in hepatogenesis. The review on radiation chimeras, by Koller, Davies, and Doak, is particularly welcome, in view of the considerable fundamental progress made in this field in recent years. The review by Creech and Krementz, on cancer chemotherapy by perfusion, deals with cancer research from a more applied angle.

The present volume appeared rather late. It is to be hoped that future volumes will again be published regularly, at yearly intervals, as was the practice previously.

I. Berenblum

Biological Alkylating Agents, *by W. C. J. Ross. Pp. xi+232. Butterworths, London. 1962. 55s. net.*

In compiling this monograph, Dr Ross is to be congratulated on having undertaken a task whose complexity must have daunted many would-be authors. The term 'biological alkylating agents' embraces compounds of such diverse chemical character as nitrogen and sulphur mustards, ethylene imine derivatives, sulphonic acid esters, and epoxides. The first part of the book discusses the fundamental chemistry and possible reaction mechanisms associated with biological alkylation. The second and larger part outlines the problems encountered in the design of anti-neoplastic drugs. As the author is an expert in this aspect of the work, he is well qualified to give a clear picture of the difficulties involved. A small section at the end is devoted to the clinical applications and limitations of these agents. The book can be recommended to the specialist and also to the worker in other branches of chemotherapy, as many of the topics dealt with, such as the principles of 'latent activity and inactivity', are applicable to drug design generally. Several mistakes were noted in the formulae; this detracts slightly from the otherwise generally good presentation of this first full-length account of the main direction of chemotherapeutic effort in the cancer field.

J. H. Lister

TUMOUR ULTRASTRUCTURE

Tumours induced by Viruses: Ultrastructural Studies, *edited by A. J. Dalton and F. Hagenau. Pp. xi+229. Academic Press, New York and London. 1962. 76s. net.*

This volume forms the first of a series devoted to ultrastructure in biological systems. It is dedicated to the memory of the late Charles Oberling and contains articles contributed by former students and personal friends on the avian leukosis complex (Hagenau and Beard); Shope papilloma (Hollmann); fibroma (Febvre); the milk agent (Moore); polyoma (Dourmashkin); mouse leukaemias (de Harven); and Moloney agent (Dalton).

In each of these articles the results of electron microscopy are studied in relation to biological aspects of the system. This layout provides a pleasant contrast to the all too common practice in such volumes of putting evidence from the electron microscope in a separate chapter, segregated from discussion of biological properties. Here, within each article, we find the biological and ultrastructural information on each system pleasingly integrated.

The monograph performs a valuable task in reviewing the recent extensive literature on the subject. It should find an honoured place in the bookshelves of all working in the field of tumour viruses, particularly if they wish to make use of electron microscopy, since the difficulties and limitations as well as the advantages of ultrastructural investigations of this type are convincingly pointed out.

D. H. Watson

VIRUS RESEARCH

Advances in Virus Research, *Vol. 8, edited by Kenneth M. Smith and Max A. Lauffer. Pp. ix+414. Academic Press, New York and London. 1962. 86s. net.*

Publications entitled 'Recent Advances' are all too often ill-digested condensations of ill-selected original papers. The present volume is a notable exception, and in fact consists of eight original essays on fundamental aspects of virology. The papers on bacteriophage are excellently illustrated and deserve wide circulation. Other papers are on plaque assay of animal viruses, contrast in electron microscopy, cytopathic phenomena and pathogenesis, mumps, and entero-viruses. There is an unusually extensive bibliography, for once including European sources, and a most competent index. This is an important contribution, and an essential reference book in any medical library.

R. J. V. Pulvertaft

PROTEIN RESEARCH

Fluorescent Protein Tracing, *edited by R. C. Nairn. Pp. xv+280. E. & S. Livingstone Ltd, Edinburgh and London. 1962. 42s. net.*

The use of fluorescent dyes conjugated to specific proteins has made it possible to detect these proteins in extremely low concentrations, and the technique is one that has a wide field of applications. Both technique and applications are described in clear and practical detail. Sources of materials and equipment are stated, together with, in many cases, their costs—a provision that will be appreciated by many an impecunious research department. Experimental applications have been dealt with by specialists in the different fields, which include direct protein tracing and immunological tracing. This work describes methods for the identification of native antibodies, and of a wide variety of micro-organisms and native antigens using fluorescent antibodies. The book, which includes forty-two photomicrographs, many in colour, is beautifully produced and is provided with a very comprehensive bibliography. It is altogether to be recommended.

D. E. Nicholson

CORTICAL HORMONES

British Medical Bulletin, *Vol. 18, No. 2, May, 1962.* The Adrenal Cortex. *Pp. 89–178. The Medical Department, The British Council, London. 1962. 20s. net.*

Since the surge of enthusiasm for the use of cortical hormones in therapy, occasioned by the demonstration in 1949 of the beneficial effect of cortisone in rheumatoid arthritis, much progress has been made in assessing the physiological effects, the therapeutic value, and the chemical interactions of adrenal cortical hormones and their synthetic analogues. The publication by the British Council of a volume on the adrenal cortex is timely indeed. Since 1949, much sobering information has curbed initial excessive therapeutic hopes; a large amount of work by organic chemists has proved that synthetic analogues of cortical hormones, far from being inferior, may be superior to the natural products for therapeutic purposes. However, as far as the fundamental understanding of the mechanism of action of these important hormones is concerned, we are further than ever from knowing the answer. This and many other aspects of the function of the adrenal cortex are reviewed in the British Council's excellent monograph. *M. Vogt*

CARBOHYDRATE BIOCHEMISTRY

Carbohydrates of Living Tissues, *by M. Stacey and S. A. Barker. Pp. xvii+215. D. Van Nostrand Co. Ltd. London. 1962. 45s. net.*

Although much current research in carbohydrate chemistry is aiming at a complete understanding of the properties of simple compounds, increasing attention in the last decade has focused on the more complex carbohydrates of living tissues. Progress was made possible by a close collaboration of the medical profession, biochemists, and research chemists. Delicate methods have been developed for the isolation of components of tissues and their structural analysis. Much light has been thrown on the biological role of such components and the changes in structure they undergo under various conditions. The findings of the investigations have been reported in numerous papers in many journals. The present monograph should thus be very much welcomed by the initiated as a handbook, and by the newcomer to this field as a comprehensive introduction.

The book is divided into eight main chapters, dealing with glycogen, hyaluronic acid, chondroitin and its sulphates, heparin and its sulphate, miscellaneous polysaccharides, milk oligosaccharides, blood group polysaccharides, mucoproteins in health and disease, and lipocarbohydrates. Each chapter gives a detailed account of our present knowledge of these substances. The book is well illustrated with diagrams of structures and reaction sequences. The reader will find little difficulty in tracing original literature, as numerous references are given. The authors, themselves experienced chemists in this field, have presented a book in which current problems are discussed with great clarity. *H. Weigel*

PHOTOSYNTHESIS

The Photosynthesis of Carbon Compounds, *by M. Calvin and J. A Bassham. Pp. xxi+127. W. A. Benjamin Inc., New York. 1962. $5.50.*

This book gives a clear and concise account of present knowledge of the reactions occurring in the green plant that are connected with the assimilation of carbon dioxide. The authors assume the presence of a source of a reduced coenzyme and of an active phosphate group and then examine in turn the biosynthetic pathways from CO_2 to the variety of carbon compounds making up the whole living plant. The section concerning balance among synthetic pathways is of special interest, for it is here strongly suggested that the older view, that there could be a single carbohydrate as the first product of photosynthesis, must be rejected. As the authors point out, their present account of carbon assimilation is concerned entirely with dark reactions; and the mechanism of the formation in light of oxygen, and the reducing and phosphorylation capacities, is not touched upon. In spite of the title, in a book of this length, consideration of the hydrogen transport mediated by the light-absorbing pigments would be out of place. The term 'photosynthesis' has always been considered as not very satisfactory by plant physiologists. The original proposal 'photosyntax' was never accepted, though it indeed expresses some kind of organization. In any case, in photochemistry itself the concern is largely with the dark processes. The authors have produced a book of value to all biochemists. *Robert Hill*

BRITISH FLORA

Flora of the British Isles *(second edition), by A. R. Clapham, T. G. Tutin, and E. F. Warburg. Pp. xlviii+1269. Cambridge University Press Ltd, London. 1962. 70s. net.*

In the ten years since the first issue of this Flora it has proved to be of enormous help to the botanists, natural historians, and others for whom it filled so long-felt a want. The issue of the same authors' 'Excursion Flora' in 1959 removed the need to make the main work fit into a shooting pocket (anything smaller was impossible), and the fortunate resolution has been taken to increase the size of the page and the thickness of the paper. The work has consequently become much easier to consult indoors or out.

Considerable revision has also been undertaken and several of the keys modified in the light of experience. Results of current investigations on variable species and 'critical groups' have been taken into account, so that the work is now as fully up to date as when it first appeared. There can be no doubt that it will be as useful and welcome in the next decade as it has been in the past. *W. O. James*

MARINE BIOLOGY

Océanographie biologique et biologie marine, *by J. M. Pérès. Vol. I,* **La vie benthique.** *Pp. viii+541. Presses Universitaires de France, Paris. 1961. 30 NF.*

While there are a number of excellent books on marine plankton, there are few general accounts of the equally important benthos. This book therefore meets a real need, as it covers the various aspects of bottom life in the sea from the deep (aphytal) zone to the illuminated shallow water and intertidal areas, which include mangrove swamps and coral reefs. A general account of the marine environment is followed by descriptions of all types of benthic organisms, with an account of their biology. Methods of investigation and the numerous ecological groups are finally described.

Adverse criticisms might include the illustrations, which are crudely executed—the greater pity because they are worthy of better treatment—while their source is frequently not adequately given. There is also no index, a very serious omission in a book covering so wide a field.

Nevertheless, the scope of this book and the wide sources of information, including much Russian research, give it real value. It should certainly be read by all who are interested in the marine benthos and be available for consultation by those more widely interested in marine biology and oceanography. Any further volume or volumes by Professor Pérès are awaited with interest. *C. M. Yonge*

OVARIAN RESEARCH

The Ovary, *Vol. I, edited by S. Zuckerman, assisted by A. M. Mandl and P. Eckstein. Pp. xiii+619. Academic Press, New York and London. 1962. £7 17s. 6d. net.*

With new biological texts appearing almost weekly, a reviewer is oppressed by the conviction that the flow is determined by publishers' profit motive rather than by scientists' needs. But every now and then, worth-while treatises do appear and help to justify this state of affairs: such a one is Zuckerman's 'The Ovary'. Knowledge of that much-investigated organ has not previously been collated in the wide context here employed.

This volume deals with 'the natural history of the ovary', the more chemical and experimental studies being contained in Volume 2. The first chapter is on ovarian development and oogenesis, and this is followed by chapters on ovarian structure and histochemistry, and on ovarian and concomitant endocrine changes in the different phases of reproductive life. There are chapters, too, on atresia and on the influence of ovarian hormones on ovum transport and implantation. A wide variety of animal types is systematically considered, ranging from invertebrates to man. The book ends with chapters on the menopause and on human clinical anomalies involving ovarian dysfunction. In general, a nice balance is maintained between detailed documentation and authoritative account.

There are few omissions of note, but R. J. Blandau's descriptive work on ovulation should have received more detailed mention than it does, and little information is given on the study of ultrastructure. Nonetheless, the book can be wholeheartedly recommended as a mine of well-organized information. *C. R. Austin*

SOIL ANIMALS

Soil Animals, *by D. K. McE. Kevan. Pp. xv+237. H. F. & G. Witherby Ltd, London. 1962. 30s. net.*

The animal life of the soil, long neglected by zoologists, has received increasing attention during the past fifteen years, and the subject has now attained such dimensions that a good comprehensive introduction to it is urgently required.

In 'Soil Animals', Professor Kevan has succeeded admirably in meeting this need. In little more than 200 pages he outlines clearly and concisely what is known of the biology of the major groups of soil inhabitants and of their interrelationships. He discusses the nature of the soil as a medium for animal life, the influence of the fauna on the soil itself, and that of human activities on the fauna. A chapter on the problems of extracting animals from soil may help to explain the former neglect of the subject. Though brief, the treatment is never scrappy, as the author keeps rigorously to what is significant and never allows his theme to become obscured by detail. Nevertheless, he invariably tells his reader where to find additional information.

Simply and interestingly written, well documented and well illustrated, this little book should be of great value to students, teachers, and research workers, and should do much to stimulate interest in that fascinating, but still mysterious, environment—the soil. *N. H. E. Gibson*

ALGAE

The Algae, *by V. J. Chapman. Pp. viii+472. Macmillan & Co. Ltd, London; St Martin's Press, New York. 1962. 35s. net.*

This book aims to cover a very large plant group and inevitably the author has had to be selective, so that justice has not been done to certain aspects. The first chapter is concerned with criteria used in taxonomy and a brief description of the major algal groups. This is followed by a short history of algal studies, most of which is concerned with taxonomy and gives little information on the most recent history, which would have illustrated the increasingly important part played by algae in physiology, biochemistry, and genetics. The main part of the book is devoted to a description of a large number of genera mainly chosen from the green, brown, and red algae. This 'type' method of procedure is one that arouses controversy and is disapproved by the reviewer, although admittedly it has advantages for elementary students. The selection of 'types' is biased by Professor Chapman's interests and results in very poor coverage of the Chrysophyta and Pyrrophyta (Chrysophycophyta and Pyrrophycophyta in this book). The remainder of the book deals with reproduction, evolution, ecology, physiology, geographical distribution, and algal utilization, and many of these topics have been so condensed that much important work of the last twenty years has been emitted. Thus, if the aim of this book is to give the student a broad picture of the algae it is not wholly successful. Although not a second edition of Professor Chapman's 'An Introduction to the Study of Algae', 1941, it clearly owes very much to this earlier work. *F. E. Round*

MOLLUSCS

British Prosobranch Molluscs, *by V. Fretter and A. Graham. Pp. xvi+755. The Ray Society, London. 1962, £8 8s. net.*

This, the latest of the long series of Ray Society publications, deals with the most primitive of the three Subclasses into which the Gastropoda are divided. The animals concerned are largely marine, with some estuarine and freshwater representatives, and a few (two only in Britain) terrestrial ones. The book has an importance far transcending its title. While it is indeed an account of British species, with no fine detail of structure, function, or ecology overlooked, it is very much more than this. It is a volume of supreme importance to all malacologists and no less to those, in both Europe and America, who are interested in the fauna of the North Atlantic.

Moreover, because more is known about this fauna than about that of any other ocean, this book could well form the pattern on which future studies of the molluscs of other temperate as well as tropical areas should be based. It is the joint work of authors who have been collaborating over the past thirty years and have been intimately acquainted with almost every species they mention. In the width of its knowledge, the precision of its writing, and the detail and clarity of its illustrations, numbering over 300, this book could not be bettered. It should have a world-wide circulation. *C. M. Yonge*

PRIMATES

Primates; Comparative Anatomy and Taxonomy. *Vol. 5,* **Cebidae,** *Part B, by W. C. Osman Hill. Pp. xxix+537. Edinburgh University Press, Edinburgh. 1962. £9 9s. net.*

This volume, the fifth in the series of Dr Osman Hill's encyclopaedic work on the Primates, deals with the two specialized sub-families, the howler monkeys and the spider monkeys, of the New World family Cebidae, and it is well up to the standard of the preceding volumes. The subtitle is perhaps an understatement of the contents, for the latter include, in addition to full details of comparative anatomy, extensive accounts of behaviour, ecology, and geographical distribution. The publishers note that nothing so comprehensive has appeared since Forbes's *Handbook of the Primates* of 1894. But whereas it was not uncommon more than fifty years ago for an author to encompass a subject of this width, it is, with the accumulation of knowledge, surely almost unique for an author to be able to do the same today. This series by Dr Osman Hill is quite remarkable in this respect, for it is clearly the result of prodigious industry. Altogether the five volumes that have so far appeared since 1953 comprise 2500 pages, and three or four more volumes are still to appear on the Old World monkeys and apes. Moreover, the series is far from just a compilation of the work of other authors—although this in itself has involved a most intensive study of all the relevant literature (the present volume contains a bibliography of about 830 references); it is also a voluminous record of the author's own meticulous studies. Hence the text has a personal character that greatly enhances its attractiveness. The illustrations, both text figures and plates, are of good quality and almost all original, while the distributional maps are clear and informative. The author deserves high praise for this work, and primatologists will look forward with eagerness to the later publication of the volumes that will complete what may truly be called a magnum opus. *W. E. Le Gros Clark*

PATHOLOGY

General Pathology *(third edition), edited by Sir Howard Florey. Pp. xv+1104. Lloyd-Luke (Medical Books) Ltd, London. 1962. £6 net.*

When a book of this size reaches its third edition in eight years it is unnecessary to say that it has supplied a need and, when the editor and contributors have taken the trouble to revise much of the last edition and to add a new section on the immunology of tissue transplantation, there is every evidence that it will continue to do so. The new subject has been entrusted to J. L. Gowans, and there are also two new collaborators. M. A. Jennings has assisted with previous editions in a smaller capacity, and A. C. Ritchie has contributed a new chapter on the classification, morphology, and behaviour of tumours.

As before, the book is based on the classical concepts of pathology. One should not turn to it for genetic and chemical deviations from the normal, for hormone idiosyncrasies, or for the more dynamic aspects of respiratory failure or the loss of acid-base control. Nevertheless, the book is imbued with the new spirit that has revolutionized all branches of the biological sciences, and the experimental approach is in evidence on every page. One could expect no less from an editor who is also President of the Royal Society, and one can only hope that his new duties will not prevent him from guiding the book through the further new editions that will undoubtedly be demanded. *R. A. McCance*

HISTORY OF TECHNOLOGY

Medieval Technology and Social Change, *by Lynn White, Jr. Pp. xii+194+10 plates. Clarendon Press; Oxford University Press, London. 1962. 30s. net.*

This book is another indication of the lengthening of historic perspective in a field where, due to the paucity of documents and the lack of the professional historian's interest, it was once assumed that nothing of importance had happened until our own time. Professor White deals—succinctly but thoroughly—with three important aspects of medieval technology. Firstly, the impact of the invention of the stirrup on the use of cavalry in combat, and on the rise of a new social class, prosperous enough to breed and feed horses, and dedicated to the martial code of feudalism. He follows this with a searching discussion, close to Marc Bloch, on the Agricultural Revolution of the early Middle Ages, with its combined improvement of the plough, the wider use of horsepower, and the beginning of three-field rotation. Finally, he treats of the rise of a power technology, which only old-fashioned economists still regard as the special creation of the industrial revolution of the eighteenth century. Professor White excels, not only in a mastery of the documents and physical relics but in acute powers of interpreting this material. His conclusions are equally relevant to the student of technics and the student of history. This is a work of alert research and interpretation worthy to be placed beside that of Marc Bloch and Bertrand Gille. *Lewis Mumford*

Some books received

(*Note.* Mention of a book on this page does not preclude subsequent review)

GENERAL SCIENCE

Calling the Laboratory. *Edited by W. A. R. Thomson. Pp. xi+112. E. & S. Livingstone Ltd, Edinburgh and London. 1962. 12s. 6d. net.*

Society. Problems and Methods of Study. *Edited by A. T. Welford, Michael Argyle, D. V. Glass, and J. N. Morris. Pp. vi+586. Routledge and Kegan Paul Ltd, London. 1962. 50s. net.*

MATHEMATICS

Introduction to Geometry, *by H. S. M. Coxeter. Pp. xiv+443. John Wiley & Sons, London and New York. 1962. 75s. net.*

ASTRONOMY

The Planet Saturn: A History of Observation, Theory and Discovery, *by A. F. O'D. Alexander. Pp. 474. Faber and Faber, London. 1962. 63s. net.*

PHYSICS

Elementary Introduction to Molecular Spectra, *by Børge Bak (second, revised edition). Pp. xi+144. North-Holland Publishing Co., Amsterdam. 1962. 30s. net.*

Elements of Infrared Technology, *Vol. I, by Paul W. Kruse, Laurence D. McGlauchlin, and Richmond B. McQuistan. Pp. xxi+448. John Wiley & Sons, London and New York. 1962. 81s. net.*

Fundamental Problems in Statistical Mechanics, Proceedings of the International Summer School on Theoretical Physics. *Compiled by E. G. D. Cohen. Pp. xii+249. North-Holland Publishing Co., Amsterdam. 1962. 40s. net.*

Lectures in Theoretical Physics, *Vol. II, by M. E. Rose and E. C. G. Sudarshan. Pp. vii+281. W. A. Benjamin Inc., New York. 1962. $3.50.*

Modern Physics, *by D. E. Caro, J. A. McDonell, and B. M. Spicer. Pp. 222. Edward Arnold (Publishers) Ltd, London. 1962. 20s. net.*

Physics of the Nucleus, *by M. A. Preston. Pp. x+661. Addison-Wesley Publishing Co. Inc., Reading, Massachusetts, and London. 1962. 113s. net.*

Polarized Light – Production and Use, *by William A. Shurcliff. Pp. ix+207. Harvard University Press, Cambridge, Massachusetts. Oxford University Press, London. 1962. 50s. net.*

Quantum Electrodynamics, *by R. P. Feynman. Pp. x+198. W. A. Benjamin Inc., New York. 1962. $3.95.*

Quantum Theory of Many Particle Systems, *by L. Van Hove, N. M. Hugenholtz, and L. P. Howland. Pp. x+249. W. A. Benjamin Inc., New York. 1962. $3.95.*

S-Matrix Theory of Strong Interactions, *by Geoffrey F. Chew. Pp. x+182. W A. Benjamin Inc., New York. 1962. $3.95.*

Studies in Statistical Mechanics, *Vol. I. Edited by J. de Boer and G. E. Uhlenbeck. Pp. x+350. North-Holland Publishing Co., Amsterdam. 1962. 86s.*

Theory of Fundamental Processes, *by R. P. Feynman. Pp. x+172. W. A. Benjamin Inc., New York. 1962. $3.95.*

Worked Examples in Physics, *by V. L. Zubov and V. P. Shal'nov (translated by Erwin Marquit). Pp. xii+341. Pergamon Press Ltd, Oxford. 1962. 35s. net.*

CHEMISTRY

An Introduction to the Chemistry of Complex Compounds, *by A. A. Grinberg (translated from the second edition (1951) by J. Rovtar Leach). Pp. xxi+363. Pergamon Press Ltd, Oxford. 1962. £5 5s. net.*

Experimental Thermochemistry, *Vol. II. Edited by H. A. Skinner. Pp. xix+457. Interscience Publishers Inc., New York and London. 1962. 107s. net.*

Inorganic Chemistry, *by J. H. White. Pp. 496. University of London Press Ltd, London. 1962. 25s. net.*

GEOLOGY

Study of the Earth. *Edited by J. F. White. Pp. viii+408. Prentice-Hall Inc., New Jersey. 1962. $3.95.*

GEOGRAPHY

Geographical Conversion Tables. *Compiled and edited by D. H. K. Amiran and A. P. Schick. Pp. xxxvi+315. International Geographical Union, Zürich. 1962. SFrs. 25.*

BIOLOGY

Microbes in Action – A Laboratory Manual of Microbiology, *by Harry W. Seeley, Jr., and Paul J. Vandemark. Pp. x+449. W. H. Freeman & Co. Ltd, San Francisco and London. 1962. 22s. net*

BIOCHEMISTRY

Practical Clinical Biochemistry, *by H. Varley (third edition, revised and enlarged). Pp. viii+689. William Heinemann Medical Books Ltd, London. 1962. 50s. net.*

ZOOLOGY

Brain and Behaviour in Cephalopods, *by M. J. Wells. Pp. 171. Heinemann Educational Books Ltd, London. 1962. 16s. net.*

A Text-book of Zoology, *by T. Jeffery Parker and William A. Haswell, Vol. II (seventh edition) revised by A. J. Marshall. Pp. xxiii+952. Macmillan & Co. Ltd, London. 1962. 70s. net.*

Taschenbuch der Zoologie. *Vol. I:* Allgemeine Zoologie, by Heinz Geiler *(second enlarged edition). Pp. viii+458. Georg Thieme, Leipzig. 1962. DM 33.70.*

MEDICINE

A Ciba Foundation Symposium on Tumour Viruses of Marine Origin. *Edited by G. E. W. Wolstenholme and Maeve O'Connor. Pp. xiii+441. J. & A. Churchill Ltd, London. 1962. 60s. net.*

A Practice of Social Medicine. *Edited by Sidney L. Kark and Guy W. Steuart. Pp. xii+372. E. & S. Livingstone Ltd, Edinburgh and London. 1962. 40s. net.*

Typhoid Fever and other Salmonella Infections, *by R. L. Huckstep. Pp. xvi+334. E. & S. Livingstone Ltd, Edinburgh and London. 1962. 42s. net.*

ENGINEERING

Automatic Control – An Introduction to the Theory of Feedback and Feedback Control Systems, *by A. E. de Barr. Pp. 118. Chapman and Hall Ltd, London and New York (published on behalf of The Institute of Physics and The Physical Society). 1962. 7s. 6d. net.*

Microminiaturization – Proceedings of the Agard Conference, Oslo, July 24–26 1961. *Edited by G. W. A. Dummer (published for and on behalf of Advisory Group for Aeronautical Research and Development, North Atlantic Treaty Organization.) Pp. x+355. Pergamon Press Ltd, Oxford. 1962. £5 5s. net.*

Optimization Techniques – With Applications to Aerospace Systems, *Vol. 5 of* Mathematics in Science and Engineering. *Edited by George Leitman. Pp. xiii+453. Academic Press Inc., London and New York. 1962. 114s. 6d. net.*

TECHNOLOGY

Barley and Malt, Biology, Biochemistry, Technology. *Edited by A. H. Cook. Pp. xiv+740. Academic Press Inc., New York and London. 1962. £7 10s. net.*

The Chemical Composition and Properties of Fuels for Jet Propulsion, *by Ya. M. Paushkin (translated by William E. Jones). Pp. 480. Pergamon Press Ltd, Oxford. 1962 £5 net.*

Chemicals from Petroleum, *by A. L. Waddams. Pp. ix+179. John Murray, London 1962. 16s. net.*

Rubber – Botany Cultivation and Utilization, *by Loren G. Polhamus (Series* World Crops*). Pp. xvii+449. Interscience Publishers Inc., New York. 1962. 80s. net.*

Synthetic Materials from Petroleum, *by A. V. Topchiev, M. F. Nagiyev, and T. N. Shakhtakhtinskii (translated from the Russian by J. Burdon). Pp. ix+128. Pergamon Press Ltd, London. 1962. 25s. net.*

AGRICULTURE

Agricultural Entomology in the Tropics, *by G. H. Caswell. Pp. 152. Edward Arnold (Publishers) Ltd, London. 1962. 21s. net.*

Evolution des sciences – sol, microflore et végétation, *No. 20. Pp. 172. Masson et Cie, Paris. 1962. 20 NF.*

The Semen of Animals and Artificial Insemination. *Edited by J. P. Maule. Pp. xviii+420. Commonwealth Agricultural Bureaux, Farnham Royal, Bucks. 1962. 60s. net.*

METALLURGY

The Influence of Temperature on the Mechanical Properties of Metals and Alloys, *by E. M. Savitsky. Pp. xii+303. Oxford University Press, London. 1962. 50s. net*

HISTORY OF SCIENCE

British Scientists of the 19th Century, *by J. G. Crowther. Pp. xii+332. Routledge and Kegan Paul Ltd., London. 1962. 12s. 6d. net.*

A Short History of Medicine, *by Charles Singer and E. Ashworth Underwood (second edition). Pp. xv+854. Oxford University Press, London. 1962. 63s. net.*

Fourcroy – Chemist and Revolutionary, 1755–1809, *by W. A. Smeaton. Pp. xvi+288. Printed for the author by W. Heffer & Sons Ltd, Cambridge. 1962. 40s. net.*

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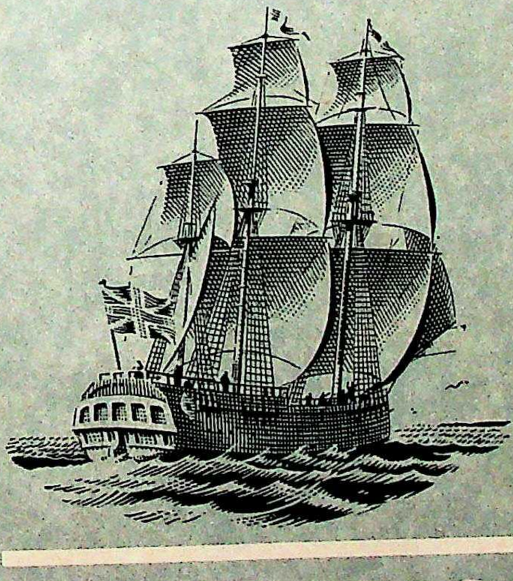
for the publishers, Imperial Chemical Industries Limited Millbank, London S.W.1



ENDEAVOUR

S. R. B
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VOLUME XXII NUMBER 86 MAY 1963

Endeavour

Endeavour has been published by Imperial Chemical Industries since 1942. It presents, for scientists throughout the world, a regular review of the progress of science. While the emphasis is on British science, contributions are regularly commissioned from all parts of the world; the principal considerations are the intrinsic interest and importance of the subject and the authority of the writer. To ensure international acceptance, the journal is published in English, French, German, Italian, and Spanish.

No charge is made for *Endeavour*, and it is distributed to senior scientists, scientific institutions, and libraries throughout the world. Within these limits, the Editor is always glad to consider the addition of names to the mailing list.

ICI

The drawing on the cover is of the bark *Endeavour*, which, commanded by Captain James Cook and carrying a number of scientific workers, was sent out by the British Admiralty in August 1768, following a Memorial by the Royal Society to King George III, to chart the South Pacific Ocean and observe the transit of Venus.

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ENDEAVOUR

VOLUME XXII MAY 1963

A review of the progress of science, published in five languages

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The International Years of the Quiet Sun

International cooperation in geophysical science reached a climax in 1957–58 with the International Geophysical Year. In this, scientists from nearly seventy countries co-operated in a vast coordinated programme of research. Elsewhere in this issue, Sir Harrie Massey reviews some of the principal achievements of this tremendous collaborative project.

The IGY was the third international enterprise of its kind. The two earlier ones were the 'Polar Years' of 1882–83 and 1932–33, which were much more limited in scope. The IGY was held after a further period of twenty-five, rather than fifty, years, and for this reduced interval there were two main reasons. Firstly, the period 1930–50 witnessed exceptionally rapid advances in certain experimental techniques, and progress was particularly marked in radio science, a field which touches closely upon many geophysical disciplines. Secondly, the 'Second Polar Year' nearly coincided with a period of minimum solar activity, and it was considered desirable to organize a new set of concerted geophysical studies at a period of maximum solar activity. During such a period, frequent solar, and related terrestrial, disturbances could be expected. As it turned out, the choice of 1957–58 for the IGY was most fortunate, in that it was a period of quite unusual solar activity. The sunspot numbers during the IGY were much larger than any previously recorded in the two centuries for which reliable figures are available.

Even in the planning stages, it was emphasized by scientists in certain fields, notably upper atmospheric physics, that there would be great value in maintaining, at least for a few years, the IGY network of stations. Subsequently, it became clear that in all those disciplines that are in any way affected by solar activity the full fruits of the IGY enterprise can be realized only if comparable data were available for a period of very low solar activity. Considerations such as these have led to a decision to conduct, during the next solar minimum period, a further full-scale international programme.

The new enterprise has officially been named the International Years of the Quiet Sun (IQSY) 1964–65. The 1882 and 1932 'Polar Years' covered periods of twelve months, and the IGY extended over eighteen months; the IQSY will cover a full two-year period, 1st January 1964 to 31st December 1965. Although many solar and terrestrial phenomena are intimately connected, and disturbances in the terrestrial phenomena closely follow, in time, disturbances on the Sun, it is found that the long-period minima in solar activity and in certain geophysical phenomena may differ by several months. The minima themselves are also 'flat' and gradual in character, and this makes it difficult to predict precisely when the quietest conditions are most likely to occur. It is in order to be quite certain that the periods of least activity in both solar and terrestrial phenomena are covered, that it has been decided to extend the IQSY over two complete years.

The studies to be made during the two years fall into three categories. Firstly, studies that can be carried out only at a period of minimum solar activity, or at least are best carried out at such periods. Secondly, studies of isolated solar and associated terrestrial phenomena under quiet background conditions. Thirdly, studies that will provide data for quiet solar conditions comparable with those obtained during the IGY.

In the disciplines concerned in the IQSY, the scientific programmes will consist of both synoptic and special observations, and it is anticipated that the network of stations will be at least as dense as that in operation during the IGY. However, the IQSY will not provide a mere repetition, under different conditions, of IGY measurements. Modifications in the network of stations, in the schedule of observations, and in the techniques employed are being introduced in the light of new knowledge gained during and since the IGY.

One of the distinctive features of the IGY was the use of rockets and satellites to provide new and direct information on the high atmosphere and on interplanetary space. Since then, these space vehicles have contributed enormously to our understanding of solar-terrestrial relationships, and it is clear that they will play an ever-increasing role in these studies. Hence the fullest possible plans are being made for an internationally conducted space-research programme during the IQSY. The major objectives in the various disciplines are briefly as follows.

The meteorological programme is designed to study the large-scale physical, dynamical, and thermodynamical characteristics of the atmosphere above the 100 mb level (about 10 miles altitude) and also the relationship between the upper and lower atmosphere. The geomagnetic programme is directed to studies of solar and lunar variations in the magnetic field, and of the geomagnetic effects of solar eclipses under the favourable conditions that should occur during the IQSY period. It is expected, too, that the magnetic observations at surface observatories, as well as in space, will contribute substantially to the World Magnetic Survey, which is a deferred IGY project. The IQSY auroral programme will provide data on any solar-cycle changes in the auroral zones and on the frequency of occurrence of different types of aurora.

The ionosphere programme is generally aimed at completing studies of the dependence of the ionosphere on the solar-cycle. The ionosphere and exosphere will be sounded to very great heights, using all the new techniques, including high-power radar, rockets, and satellites. In the solar activity programme, the solar patrol, both optical and radio, initiated during the IGY will continue. In addition to ground observations, satellite-borne photometers and spectrographs will monitor solar radiation in the ultraviolet and X-ray regions of the spectrum. The cosmic-ray programme has a number of objectives, including investigation of the emission of energetic particles by the Sun at minimum activity and the study of their mode of propagation through the interplanetary magnetic field. The energy spectrum and composition of the low-energy cosmic rays that are unable to reach the Earth at times of high solar activity will also be investigated.

The solar minimum period is particularly appropriate for determining the value of many physical parameters of the Earth's atmosphere such as pressure, density, temperature, mean molecular mass, and chemical composition.

Soon after the close of the IGY, the International Council of Scientific Unions decided to establish a permanent International Committee for Geophysics (CIG), and it is this committee that has been entrusted with the planning and organization of the IQSY. Following the pattern adopted for the IGY, the programme recommendations are being formulated by a group of scientists who serve as international reporters for their disciplines. The organizing committee also includes representatives of the World Meteorological Organization and of various other international scientific bodies, such as the Committees for Space Research, Antarctic Research, and the World Day Service.

The President of the International Committee for Geophysics and of the International Years of the Quiet Sun enterprise is Professor W. J. G. Beynon of the United Kingdom, and the Secretariat has been established in London. The observational work, to be carried out at many hundreds of stations, will involve the voluntary cooperation of scientific academies and institutions of more than sixty nations. The information collected will be shared through the World Data Centres.

Mechanoreceptors

T. A. Quilliam and J. Armstrong

The skins of higher animals have a structurally diverse nerve-system by which they can detect mechanical events caused by contact or by pressure waves. Because of their characteristic structural organization, certain types of cutaneous transducers (corpuscles) may propagate nerve impulse signals only in response to particular components, such as specific vibration frequency bandwidths, of the complex stimuli produced by such events. This article describes a number of types of corpuscle and discusses their use to the various animals concerned.

Introduction

In fishes, the sensory nerves to the skin consist of fine bare fibres that branch to form open-meshed networks before terminating among the most superficial living cells. Such a fibre system presumably serves to provide these animals with the sort of information about the outside world that human beings might interpret as either touch or pain. Fishes seem to have no structurally specialized peripheral receptors for signalling separately the occurrence of events that must be avoided (pain) and of those that may perhaps profitably be pursued (pressure and touch). In higher forms, the signalling of tissue injury and its consequences seems to remain a function of fine superficial nerve-fibre networks of the skin, but most of these animals have in addition a variety of more differentiated transducers.

A number of reptiles and amphibians possess raised plaques, on the skin of their head or tongue, that are liberally supplied with relatively unspecialized nerve endings. These regions are probably more sensitive to certain environmental changes than is the rest of the body surface, but we know little of their modes of action. Birds and mammals have dense nerve plexuses round the roots of the feathers or hair in the deeper layers of the skin (figures 1 and 2). The long feather or hair functions as a lever. Gentle displacements of its free end will produce a more powerful distortion at its root, and this may be sufficient to generate signals in the surrounding nerve networks. Cats and other mammals have very long whiskers (vibrissae, or sinus hairs) that are specialized to form teletactile organs that seem able to detect approaching objects, presumably by responding to pressure waves set up in the air [1].

The actual nerve terminations in other organized sensory nerve endings (corpuscles) of higher animals are also closely associated with cellular components of a non-nervous character. Such endings are probably collectively responsible for the wide range of transcutaneous sensibility that is characteristic of higher animals, reaching a particularly high degree of sophistication in man.

There is an element of truth in the assertion that it is the outstanding development of the human brain that is alone responsible for man's pre-eminence in the field of tactile discrimination. However, the fact remains that in those skin areas, such as the finger-tips, that man uses to explore his environment, an array of corpuscles of several special types is found, each type being very abundant. These include the Meissner corpuscles—perhaps recording movements of skin ridges [2], Merkel disk corpuscles (figure 15), and deeper-lying Pacinian corpuscles (figure 3). In addition there are many simpler varieties of nerve endings. Certain other animals also possess a special receptor array, but their brains are relatively simple. One such is the mole, which has very poor eyesight and thus depends mainly on tactile sensation for navigation both on and below the ground surface.

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Specificity

Ideas about how sensory nerve endings in the skin enable us to distinguish between different kinds of environmental change owe much to the work started by von Frey in 1894. He proposed that specific stimuli, such as touch, pain, warmth, or cold, each activated only one single morphological type of corpuscle. At that time, it so happened that the number of types of corpuscle described in the literature was roughly equal to the number of modalities of transcutaneous sensation then recognized. However, more recent work has brought to light many facts about skin sensation that cannot be easily explained by so simple a hypothesis [3]. Even though some workers believe that it is always possible to recognize three broad morphological types of ending in the limbs of man, other studies indicate that there is a continuous spectrum of sizes and shapes of nerve ending, and that the classical types of corpuscle have been artificially isolated from an unbroken range.

Lamellated corpuscles

An especially striking form of transducer is the lamellated corpuscle found superficially in the skin or deeper in certain of the other tissues. Those found in mammals are called Pacinian corpuscles (figure 3), and those in birds are known as Herbst type corpuscles (figure 4). The former are sensitive to mechanical displacement and thus to vibration, and the many similarities in structural design between these two types of corpuscle strongly suggests that the latter, too, are sensitive to vibrations. Their function supplements, rather than duplicates, that of the inner ear, which normally detects only airborne vibrations.

Unfortunately, little is known about the actual transducer mechanism by which deformation of a corpuscle evokes the propagation from it of nerve impulses. Consequently the precise part that the lamellae play in corpuscular functioning is uncertain, but presumably their number and arrangement serve to make each type of corpuscle a detector of special sensitivity for some specific type of pressure application or range of vibrational change normally transmitted through the surrounding soft tissues. The lamellae may do this either by protecting the nerve terminal that they surround against changes other than those to be detected, or, conversely, by making the nerve terminal especially sensitive to one particular type of stimulus only.

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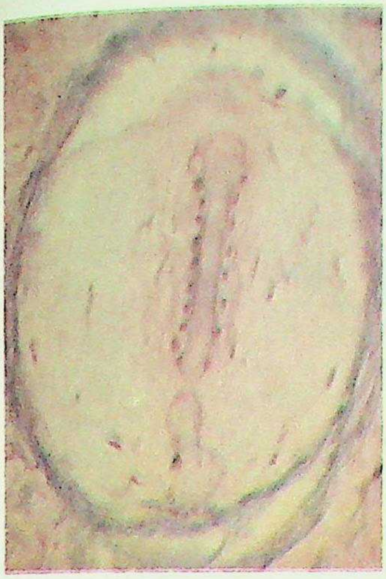

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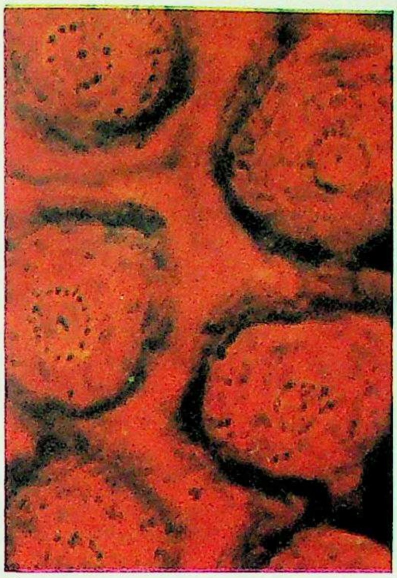

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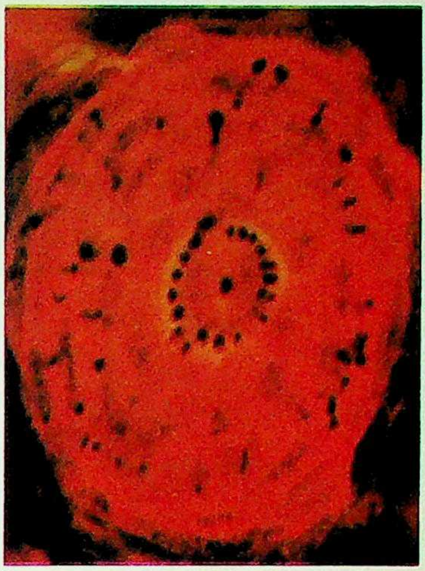

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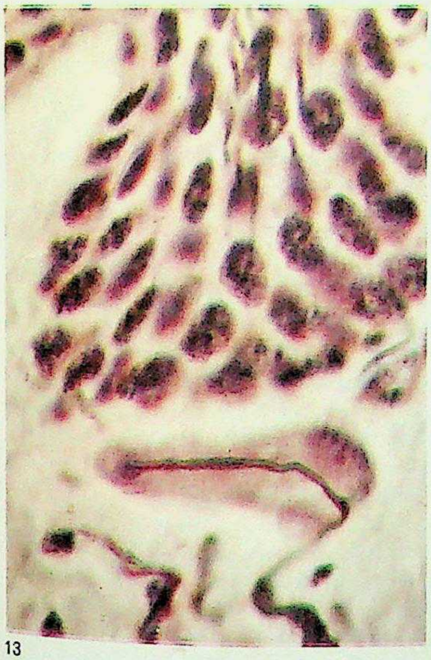

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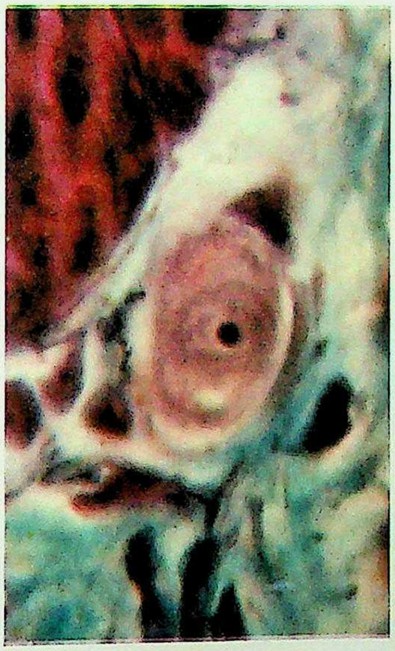

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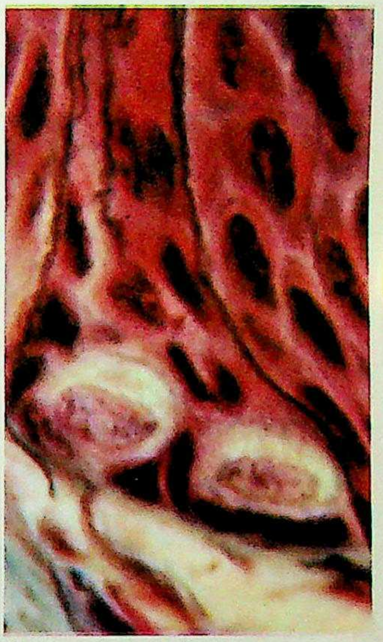

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Figure 1 *Root of mole vibrissa cut transversely. A plexus of nerve fibres surrounds the hair shaft with its inner sheath. (×600)*

Figure 2 *As figure 1. At a lower level, a ring of small nerve fibres (like minute markings on a clock face) surrounds a double hair shaft with associated inner sheaths. A blood sinus and an outer capsule encircle these structures. (×420)*

Figure 3 *Pacinian corpuscle (cat pancreas). (×100)*

Figure 4 *Herbst corpuscle (skin of duck's bill). (×375)*

Figure 5 *Herbst (large) and Grandry (small) corpuscles (skin of duck's bill). (×65)*

Figure 6 *Grandry corpuscle (skin of duck's bill). (×1600)*

Figure 7 *Transverse section through Pacinian corpuscle to show inner core hemilamellae, clefts, and central nerve terminals. (Cat pancreas.) (×1000)*

Figure 8 *As figure 7, after nerve interruption. (×1200)*

Figure 9 *Ultraterminal processes of nerve ending (Pacinian corpuscle, cat pancreas). (×1000)*

Figure 10 *Herbst corpuscle after nerve interruption (skin of duck's bill). (×500)*

Figure 11 *Horizontal section through tip of mole's snout to show the close packing of Eimer's organs. (×400)*

Figure 12 *Section of an Eimer's organ, showing central and satellite nerve terminals embedded in epidermal cells. (×1000)*

Figure 13 *Lamellated nerve ending lying below an Eimer's organ, seen cut in a vertical plane. (×750)*

Figure 14 *As figure 13, in another vertical plane. (×1500)*

Figure 15 *Two Merkel disk corpuscles at base of an Eimer's organ, cut vertically. (×1800)*

The ordinary fibres of a peripheral nerve trunk are sensitive to mechanical stimuli. Interestingly enough, its thick 'mature' nerve fibres, which are protected by several protoplasmic and fibrous sheaths, are much less sensitive than its thinner ones, which are not so well sheathed. Again, the extremely thin tips of fibres growing out from the proximal segment of a severed nerve trunk are particularly sensitive to mechanical stimulation. This latter fact can be confirmed during the recovery in a patient with a damaged peripheral nerve trunk. The constantly advancing level reached by regrowing fibre tips can be identified, as recovery proceeds, by tapping lightly on the skin along the course of the distal segment of the nerve. A characteristic tingling is felt over the region that has most recently been reached by the newly growing fibre tips (Tinel's sign). This sensation cannot be obtained over the more mature parts of these same fibres, which have acquired sheaths, nor peripherally where the original nerve fibres, bereft of connection with their cell bodies situated in or near the spinal chord, have degenerated.

The importance of these facts in the present context is that they suggest that it is the presence or the absence of various types of sheath that determines whether a given type of lamellated corpuscle will be sensitive to a lesser or to a greater extent to particular mechanical components of a complex environmental stimulus. Moreover, a single lamellated corpuscle can seldom be activated alone. Any important environmental change is probably signalled to the brain by the joint 'discharge' of several individual corpuscles in one locality or even by groups of corpuscles in different sites. This information could supply clues about the proximity or direction of the source of the stimulus. Corpuscular structure varies slightly in various species, and different patterns of topographical distribution occur. Thus, corpuscles may be found alone in one tissue and associated with various other types of nerve ending in another. Each such array of nerve endings signals the occurrence of those specific components of a complex stimulus that are of 'interest' to a particular type of animal.

The Pacinian corpuscle

The existence of this type of lamellated nerve ending was first recorded in 1741 in a thesis on human anatomy by Lehmann, who worked in Vater's department in the University of Wittenberg. Nearly a century later, in 1835, Pacini described these structures much more fully to the *Società Medico-Fisica* of Florence. He published his classical work, which included the results of a microscopic study and of simple micromanipulations, in 1840.

The corpuscles are ellipsoidal bodies large enough (up to 2 mm × 0·5 mm) to be seen with the naked eye. They occur in many species of animals and in different parts of the body. In man, they are very numerous in the finger-tips, lying rather deeply in the skin, and they occur also in the coverings of muscles and tendons. In the cat, they occur in the paw pads, on the membrane uniting the bones of the shank, in the mesentery (the tissue folds that support the gut), and in the pancreas. It is not easy to see the common factor in this list of situations. In various other animals, lamellated corpuscles have also been reported in the walls of the urinary tract and in relation to blood vessels. They occur also in the tail of a monkey, the wing of a bat, and in the external genitalia. They are found in relation to various ducts and even near the channel that drains the anterior chamber of the eye. Thus, besides signalling vibrations emanating from external sources, it seems likely that they can also monitor fluid flow within the body, perhaps by recording either the pressure changes which accompany peristaltic activity or the vibrations that are produced when blood, for example, circulates rapidly through narrow elastic channels, especially those possessing valves or sphincters.

Morphology

Basically the Pacinian corpuscle consists of a central nerve terminal surrounded by a series of three sets of thin concentric protoplasmic sheets or lamellae. The outermost of these is called the capsule (2–3 μ thick) and consists of up to eight thin concentric lamellae of protoplasm reinforced externally by irregularly orientated collagen fibrils. Within this is an extensive 'outer zone' of some 60 thin concentric protoplasmic lamellae supported by collagen fibrils each separated by a fluid-filled space from its neighbours. The lamellae are very thin imperforate multicellular shells (figure 16), and the spaces between them make up over 90 per cent of the volume of this region.

The inner core (figure 7) differs from the outer in consisting of up to 80 protoplasmic hemilamellae. These are much more closely packed, so as to be without intervening fluid or collagen fibrils. Its characteristic symmetry is based on a pair of radial clefts and, axially, on the nerve terminal. These, together, separate the hemilamellae into two stacks [4]. Consecutive lamellae are always derived from different cells. This alternation may prove to be a significant feature of the functional organization of the inner core. The structural pattern of this system of hemilamellae is thus very different from the continuous series of spirally wound lipoprotein membranes that make up the myelin sheath surrounding all but the smallest nerve fibres elsewhere in the body. Those membranes are formed by the rolling up of the surfaces of satellite cells (Schwann cells) and the squeezing out of cytoplasm between the rolled-up surfaces.

The cells of the inner core in the Pacinian corpuscle may perhaps correspond to Schwann cells. However, this is uncertain, as there appears to be no increase in the number of nuclei in the inner core region after the nerve fibre supplying the corpuscle has been interrupted (figure 8), as occurs in Schwann cell populations of damaged peripheral nerves [5].

The nerve fibre loses its myelin sheath just before its entry to the inner core and undergoes certain structural modifications that may prove important in delineating the end of the conducting segment of the nerve fibre and the start of the vibration-sensitive terminal that follows the long axis of the corpuscle distally for 600 μ or more. It ends at the distal pole of the inner core in several club-like processes (figure 9). The outline of the terminal is smooth, but in cross section it is oval. Its longer transverse diameter coincides with the plane of the cleft (figures 7 and 16). Electron-microscopic studies show that the terminal itself contains many mitochondria arranged peripherally and also, near the cleft region, a number of small bodies ressembling synaptic vesicles [4]. Evidently, the terminal is the site of intense metabolic activity, but the precise nature of this is as yet uncertain.

Physical distortion of the membrane bounding a nerve terminal has been proposed as a likely-primary mechanism responsible for initiating nerve impulses [6]. The oval shape of the nerve terminal might thus have a practical significance; compression forces that act equally along any axis would alter the surface area of an oval cylinder to a greater degree than that of a true cylinder [7].

Function of Pacinian corpuscles

There is firm evidence that the Pacinian corpuscle signals the occurrence of mechanical vibration [8]. For isolated corpuscles

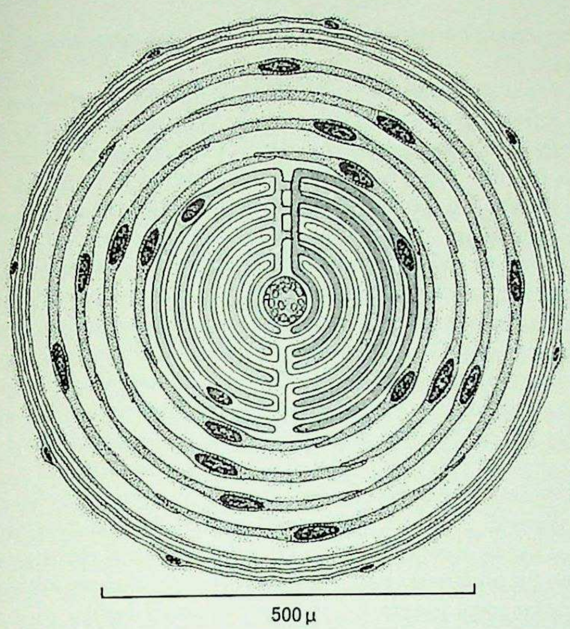

Figure 16

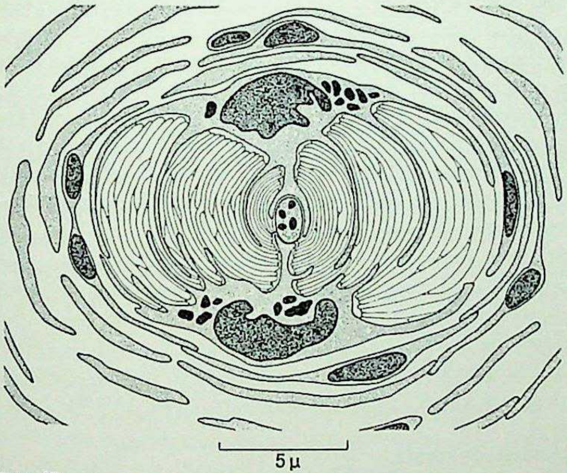

Figure 17

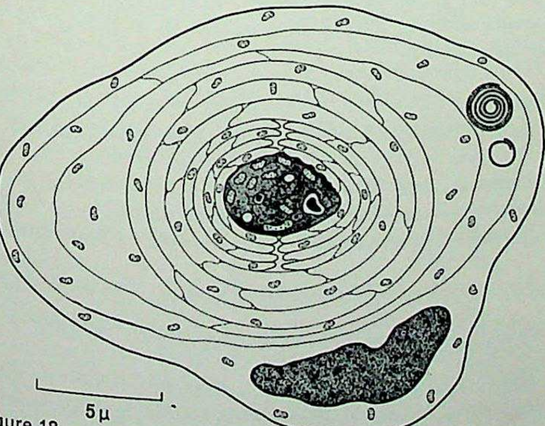

Figure 18

Figure 16 *Structural organization of Pacinian corpuscle. (Number of lamellae are drastically reduced for clarity; transverse section not drawn to scale.)*

Figure 17 *Diagram of electron-microscopic appearance of the inner core region of Herbst corpuscle. (Cut transversely.)*

Figure 18 *As figure 17. Lamellated corpuscle from mole.*

taken from the mesentery of the cat, the maximum sensitivity to sine waves lies near 400 c/s [9]. There is no response to frequencies below about 50 c/s and little to frequencies in excess of 600 c/s (figure 19). Presumably the arrangement and constitution of the lamellae and intervening fluid lakes endow the corpuscle with this 'bandpass filter' property.

In laboratory experiments, isolated Pacinian corpuscles have been shown to respond to vibrations caused by people walking about nearby. In domestic situations, the cat may use the Pacinian corpuscles in its paws and legs to detect vibrations caused by the movements of an unseen and inaudible mouse. If the signal strength increases, for example when the mouse approaches or when the cat lies on the floor, the corpuscles in the abdomen may be activated as well.

The Herbst corpuscles of birds

These are found in or on the membranes covering and uniting the bones of the legs and in the skin near the feather roots, and in particular profusion in the skin of the bill of aquatic birds (figures 4 and 5). Here they are associated with only one other type of nerve ending. This is an encapsulated form known as the Grandry corpuscle (figures 5 and 6).

The Herbst corpuscles are about one thousand times less bulky than their mammalian counterparts, the Pacinian corpuscles. Nevertheless, the capsule of the Herbst corpuscle is more curved, two or three times thicker, and considerably stiffer than that of the Pacinian corpuscle. It consists of four to eight comparatively thick cytoplasmic lamellae interlaced with collagen fibrils and reinforced externally by several additional layers of collagen arranged so that the fibrils lie at right angles to one another.

The outer zone is made up of about ten irregularly concentric perforated lamellae, so that even though they frequently join each other and they have a considerable stiffening of collagen, the whole zone seems to be less highly organized than in the Pacinian corpuscle. Thus any selective 'bandpass' action that this zone could exercise on incoming vibratory stimuli is likely to be less specific than in the Pacinian corpuscle, and the corpuscle as a whole might be expected to exhibit comparatively wide acceptance-characteristics as far as transmitted mechanical waveforms are concerned.

Deaf bullfinches (*Pyrrula*) can develop conditioned-reflex responses to vibration of the perch that indicate a sensitivity over a wide high-frequency range, presumably through the action of this type of corpuscles in the legs [10] (figure 19).

The 'sentinel' nuclei of the cells that provide the hemilamellar units of the inner core (figure 17) are arranged as two bilaterally symmetrical rows, one on either side of the nerve terminal. They are a prominent feature under the light microscope, and distinguish avian from mammalian lamellated corpuscles (figures 4 and 3). These nuclei do not increase by division during and after degeneration of the nerve terminal [11] (figure 10) and are thus unlikely to belong to conventional Schwann cells.

The Grandry corpuscles intermingled with the Herbst corpuscles are not lamellated but have a well marked capsule. This encloses a remarkable fan-shaped disk of axoplasm (figure 6), which the electron microscope shows to be sandwiched between two satellite supporting cells. During degeneration of the nerve fibre, the capsular cells appear to multiply, although the satellite cells apparently do not.

No theory is available as to the type of stimuli to which Grandry corpuscles respond, nor is it clear just how their activities are connected with those of the Herbst corpuscles with which they are topographically associated. Perhaps

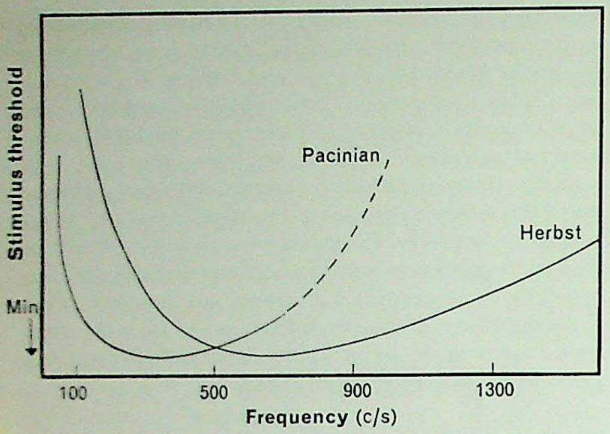

Figure 19 *Comparison of the response characteristics to vibration of the Pacinian and Herbst type lamellated corpuscles (simplified).*

Grandry corpuscles perform functions comparable to those of bare intra-epidermal endings and Merkel disk corpuscles elsewhere. Once again we see the suggestion that several types of transducer co-operate in determining sensitivities. With this array of nerve endings in its bill, the duck is presumably able to detect water-borne vibrations set up by aquatic life. Paddling on the surface of a pond may also set up vibrations that could be reflected back to the animal by solid underwater objects.

Other birds use similar corpuscles in various ways. The woodpecker (*Dendrocopus*) drums rhythmically and spasmodically on trees with its beak. This activity has several uses, but no doubt one of these is the search for food. The tongue contains many Herbst corpuscles and may be placed on the bark during drumming to detect resonance effects indicative of the presence of cracks and crannies. The bird could insert its very long tongue into the crack it then discovers, and detect by touch, and extract, boring insects that are hidden within.

Eimer's organs of the mole

An entirely different but equally elaborate array of receptors is found on the tip of the snout of the mole (*Talpa*). Here there are many small raised epidermal papillae, each of which overlies a blunt rod-like process of epidermis, which penetrates for some distance into the underlying dermis. Passing superficially through each epidermal rod from a nearby nerve plexus in the dermis are one or two thin axial nerve terminals surrounded by a ring of twenty or more satellite terminals (figures 11 and 12).

Another type of organized nerve ending found in Eimer's organ is the Merkel disk corpuscle (figure 15). Two or more are situated in the deepest layers of each rod-like epidermal processes. A single large myelinated nerve fibre enters each such corpuscle to terminate as a whorled disc of axoplasm which lies in a large fluid-filled vesicular cell.

Deep in each Eimer's organ is an unnamed lamellated corpuscle [12] (figures 13 and 14). Its capsule is not well defined, and the outer zone consists of five or six closely packed multicellular protoplasmic lamellae. There is no intervening fluid, and no collagen fibrils are present. A similar number of paired hemilamellae make up the inner core, which is somewhat irregularly arranged; clefts, although present, are not easily distinguished. The general impression is that of a very small simplified version of the basic Pacinian corpuscle design (figure 18).

Distant mechanical events affecting the soil in contact with the skin surface of the snout may be conducted direct to the deeply lying lamellated corpuscles by the stiff rods of epidermal cells forming Eimer's organs. Attenuation of the stimulus by the intervening soft tissues of the dermis would thus be minimized, and the animal's direction-finding powers enhanced. The mole would thus be enabled to detect the presence and locate the position of the earthworms or insects on which it feeds, even though they were moving about in the soil some distance away. The lamellated corpuscles might also prove to be the input channel of a vibratory 'probe' whose output source might be the animal's own digging movements. Advance teletactile information as to the nature of the earth about to be tunnelled into would thus be continuously available.

Detailed tactile information about the texture of the soil locally and of objects encountered on its subterranean travels must also be encoded by the other nervous units of this receptor array for submission to the brain as propagated nerve impulses for subsequent integration with other sensory inputs.

Significance of arrays of mechanoreceptors

It seems to be characteristic of the more specialized receptor arrays of the skin that they include several kinds of transducer. There are two sorts in the duck's bill; three, or possibly four, in the mole's snout; and in our own fingers there are three specialized types of transducer in addition to a number of simpler ones. Presumably the significance of these arrays is that by the activation of their units in various combinations they enable the skin to signal the occurrence and location of a wide range of environmental events.

Study of the receptor combinations in animals with special functional capacities should help us to understand how the various signals interact. The efficiency and versatility of the mechanoreceptors that are already much used in industry might be improved by the use of arrays of diverse transducers such as are found in living mechanoreceptor systems.

Acknowledgments

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Polonium

K. W. Bagnall

Polonium was discovered and named by Marie Curie, and was shown to be a member of the sulphur group of the Periodic Table. Very little was known about the element until recently, as natural polonium is extremely rare and is radioactive, with a relatively short half-life. Reasonable quantities of the element can now be prepared by neutron-bombardment of natural bismuth. Even so, the element is so toxic that its study demands special precautions. This article describes the chemistry of the element and some uses for it, one being as a source of energy in artificial satellites.

The chemistry of some of the rarer heavy elements was little known before the development of the atomic-energy industry, largely owing to the difficulty of obtaining weighable amounts of them for research purposes. A few of them can now be synthesized in fair quantity by neutron irradiation of commoner elements in nuclear reactors and, as larger quantities have become available, some industrial uses have been found for them. One of these elements, polonium, hitherto available only in invisible quantities, has been the subject of a good deal of investigation in the past fifteen years. Its chemistry is now quite well established, even though the preparative work has usually been carried out with submilligram amounts of material because of the hazards caused by its radioactivity. The historical background and some of the more important details of the chemistry of polonium are described below, together with some aspects of the problems of handling such a highly radioactive element.

Historical

Following the discovery of the phenomenon of radioactivity in uranium by H. Becquerel in 1896, itself a consequence of the discovery of X-rays by W. Röntgen a few months earlier, some effort was devoted to the investigation of the heavier elements and their ores in order to ascertain whether radioactivity was a general property of matter. Thorium was the next element found to be radioactive, and then, while working with uranium ores, Marie Curie observed that the radioactivity of the minerals exceeded that to be expected from their uranium content. Suspecting the presence of unknown, highly radioactive species, she, and later her husband, processed vast quantities of uranium-ore residues by methods based on conventional chemical group separations, finally obtaining invisible quantities of a highly radioactive element [1]. She subsequently named this 'polonium' in honour of her native Poland. This was the first time a new element had been discovered by methods that depended solely on observations of its radioactivity. The discovery of radium followed shortly afterwards.

Polonium was ultimately shown to be the higher homologue of tellurium predicted by Mendeleev, and hence a member of the sulphur group. However, unlike the other members of the group, no stable or long-lived isotopes of the element are known in nature. The only readily accessible isotope is the penultimate member of the radium decay series, polonium-210. This decays by alpha emission with a half-life of 138·4 days:

$$^{210}_{82}\mathrm{Pb} \xrightarrow[\text{22 years}]{\beta} {}^{210}_{83}\mathrm{Bi} \xrightarrow[\text{5 days}]{\beta} {}^{210}_{84}\mathrm{Po} \xrightarrow[\text{138·4 days}]{\alpha} {}^{206}_{82}\mathrm{Pb}$$

Polonium is one of the rarest natural elements—its abundance is only 0·2 per cent of that of radium—and uranium ores contain only about 100 micrograms of the element per ton. Thus the discovery of polonium by Madame Curie was a remarkable feat, particularly in view of the limited experimental techniques available to her at the time.

Until recently, polonium could be obtained only from uranium or its ores; from radium, which contains 0·2 per cent by weight of polonium at radioactive equilibrium; or from spent radon ampoules, which, after the radon has decayed, contain lead-210 and its daughters. Because of the difficulty of obtaining weighable amounts of polonium from these sources, all the earlier experimental work with the element was carried out on the trace scale, using quantities of from 10^{-10} to 10^{-6} g, apart from one larger quantity of about 100 μg of the element that was prepared by Marie Curie and A. Debierne in 1910 [2]. Chemical studies were therefore restricted to observations of the co-precipitation of polonium with chemically similar elements, such as tellurium; to its electrochemical behaviour in the presence of various reagents; and to its behaviour on centrifuging in different media. In every case the polonium was followed in its reactions by observation of its radioactivity, and it was not possible unambiguously to identify any chemical compounds by chemical analysis, because of the very small quantities of the element which were used. Nevertheless, later work with weighable amounts of polonium has generally confirmed the deductions made by the earlier workers from these trace-scale experiments.

In 1934, it was found that polonium-210 could be synthesized by the neutron bombardment of natural bismuth ($^{209}\mathrm{Bi}$). This yields bismuth-210, the parent of polonium in the radium decay series. In this way milligram amounts of polonium can now be prepared by using the high neutron-fluxes that are readily accessible in nuclear reactors. Nearly all the recent work with the element has been carried out in the atomic-energy establishments of the United Kingdom, the United States, and France, using polonium produced in this way.

Twenty-seven isotopes of polonium, from mass 192 up to mass 218, are now known; the only very long-lived isotopes are those of mass 208 (half-life 2·9 years) and 209 (half-life 103 years). These can be prepared by alpha, proton, or deuteron bombardment of lead, or bismuth, in a cyclotron. They would be more useful than polonium-210 for chemical work because their lower specific activity (that is, quantity of radioactive emission per unit mass) would greatly reduce the radiation effects. Unfortunately, these two isotopes are expensive to produce and have not yet been prepared in sufficient quantity for general use in research.

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Was born at Southampton in 1925 and was educated at St Paul's School, London, and Queen Mary College, University of London. He joined the Atomic Energy Research Establishment at Harwell as Scientific Officer in 1951, and he is now a Senior Principal Scientific Officer. In addition to numerous papers on the chemistry of polonium and of the actinides, he has also published 'The Chemistry of the Rare Radioelements', in 1957. He was awarded the Corday-Morgan medal of the Chemical Society in 1956 for his work on polonium.

Health hazards

The main danger in handling alpha-active material is that ingestion of even small amounts of such material may be fatal because of radiation damage to any organs in which the radioactive material may be selectively retained. The damage arises from the complete absorption of the alpha-particle energy by the tissue concerned. There is evidence, in the case of polonium, of its retention in the spleen, the kidneys, and the liver, and the maximum permissible body-burden, or tolerance, for ingested polonium is only 0·03 microcuries. This represents a particle weighing $6{\cdot}8 \times 10^{-12}$ g, about 2×10^{10} atoms. The high toxicity of the isotope becomes more apparent when one compares the maximum permissible concentrations in air of some of the better-known poisons with that for polonium-210. The safe limit for carbon monoxide is 100 mg/m^3, that for hydrocyanic acid is 10 mg/m^3, while that for polonium-210 is only 4×10^{-11} mg/m^3 [3], which makes polonium-210, weight for weight, $2{\cdot}5 \times 10^{11}$ times as toxic as hydrocyanic acid.

It is clear that any work with weighable amounts of polonium-210, representing some tens of million times the tolerable amount, must be carried out under strict control in a totally enclosed system of some kind, usually a glove-box. This is effectively a well-ventilated miniature laboratory bench, maintained under slightly reduced pressure relative to the laboratory in which it is situated, so that any flow of air that occurs is into the glove-box. This prevents the escape of radioactive material, as dust or vapour, from the box into the laboratory. The air extracted from the glove-box in this procedure must be passed through high-efficiency filters before discharge.

The equipment within the glove-box is handled in the normal way by means of rubber shoulder-length gloves which are fixed to the Perspex face of the box. Unfortunately, polonium penetrates these gloves in a few days. Gloves made from natural rubber are permeable, and it is always necessary to wear thin surgical gloves as an additional protection against contamination. The handling of small, fragile articles, such as X-ray capillaries, needs a good deal of practice and patience under these conditions.

The glove-boxes used for work of this kind have been fully described in the reviews of the chemistry of polonium [4–6], which also include much more complete accounts of the work that has been carried out with the element and of the ways in which the handling problems have been overcome.

Radiation effects

The most spectacular of all radiation effects is the blue glow that highly radioactive materials appear to emit. This is due to the excitation of the surrounding gas by the emitted particles or radiation and is accompanied by a marked fluorescence in glass or quartz where these materials are used to contain the radioactivity; reference 4 shows a good example of the glow from a few curies of polonium. The containers of such sources are noticeably hot to the touch, the heating being due to the energy given up by the particle or radiation on passing through matter. In the case of alpha-emitters such as polonium, the alpha particles are stopped completely within the solid source and its container, and give up all their energy. Calculation shows that the power released in this way by polonium-210 amounts to about 140 watts per gram of the metal. This high energy-output is useful for the rapid absolute determination of polonium by calorimetry. It has also attracted some attention for use as a convenient light-weight heat-source for thermo-electric power in space satellites.

The high levels of alpha radiation complicate work in aqueous solution with milligram amounts of polonium. This is because the radiation decomposition of the solvent in solutions containing as little as 0·2 mg of the element per millilitre causes a visible evolution of gas, and because the radiolysis products are chemically extremely active. One of them, hydrogen peroxide, rapidly oxidizes bivalent polonium and reduces the sexavalent state; the final products are in the stable quadrivalent state, so that it is difficult to study solution chemistry in any other valency state. The nature of the problem is shown more clearly by considering some studies of the electrode potential of polonium. A fine gold wire coated with 200 μg of polonium was used as the polonium electrode [7]. This electrode dissipated 31·6 milliwatts of power and the polonium gave rise to an alpha-particle flux of 10^{11} alpha particles per cm^2 per sec across the surface of the electrode, causing the disruption of about 10^{15} solvent molecules per second in the electrode layer. Surprisingly enough, the results were reasonably consistent and confirmed the earlier work using trace quantities, which had shown that polonium lies between tellurium and silver in the electrochemical series.

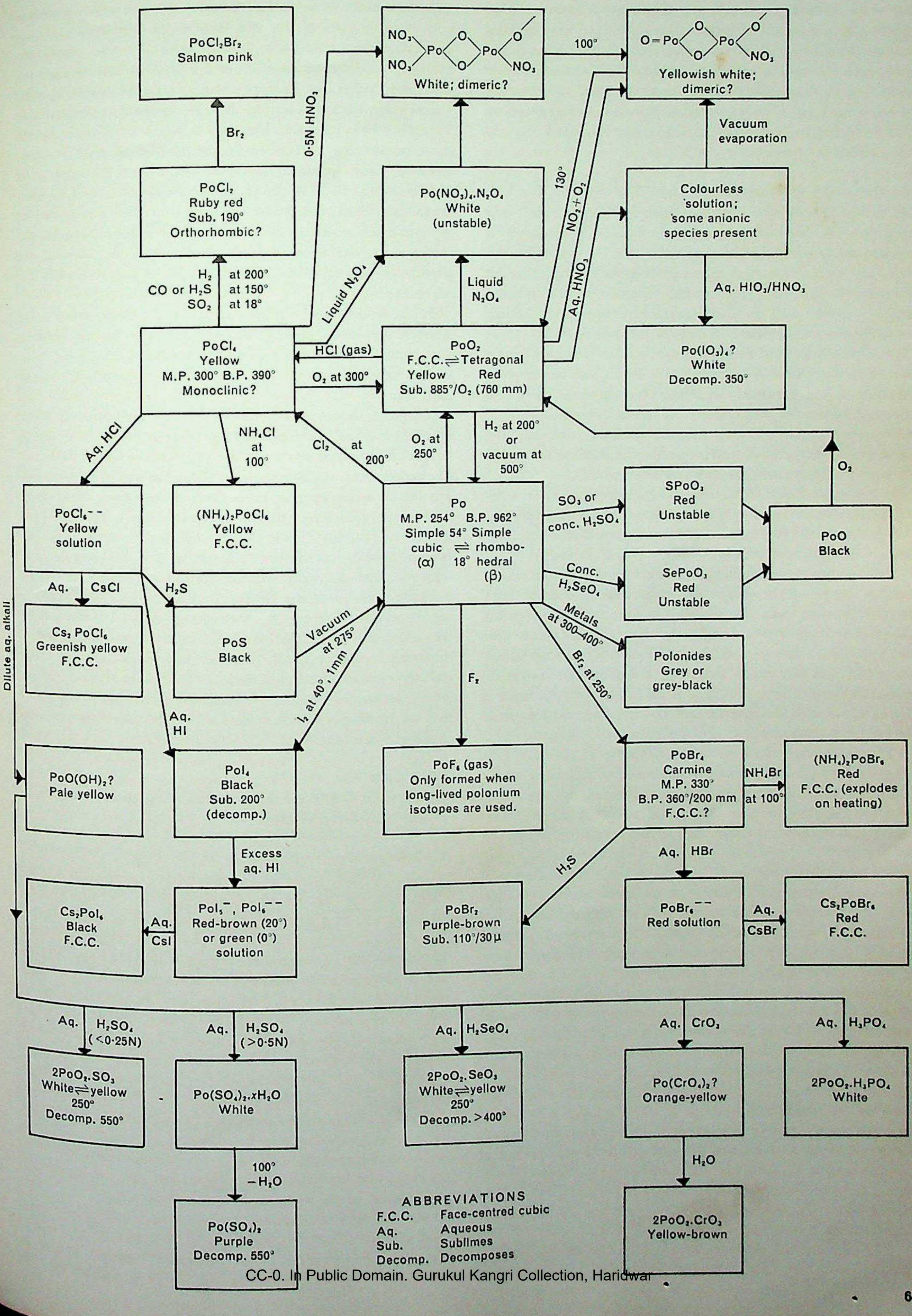
The effects of the radiation on solids include both decomposition and synthesis. Thus polonium salts of organic acids char rapidly; the iodate evolves free iodine and the halide ammines are reduced to the metal. This last reaction is probably due to atomic hydrogen liberated from the ammonia in the molecule. Polonium metal is also formed in the same way from polonium hydroxide and some other polonium compounds in the presence of concentrated aqueous, or anhydrous liquid, ammonia [8]. Synthesis of a basic polonium nitrate occurs when polonium or its halides are allowed to stand in air. This results from reaction with the oxides of nitrogen that are formed by the alpha irradiation of the air. Another example is the formation of a mixture of the two quadrivalent sulphates from moist polonium sulphide (PoS), probably by reaction with radiolytic hydrogen peroxide, a reaction that may be analogous to the corresponding oxidation of lead sulphide. The alpha radiation also disrupts the lattices of crystalline polonium compounds, so that X-ray powder photographs of these are usually of poor quality. Glass in contact with solid polonium or its compounds crazes after a few days, adding another hazard to work with the element, since the change increases the fragility of the glass. This is one of the reasons for storing high-level sources in double-walled containers.

Experimental techniques

The major part of the work recorded in the past decade has dealt with the preparative chemistry of the element and has been carried out with weighable amounts of polonium; in most cases X-ray powder photography has been used to provide or complement the analytical results. The techniques used for this work were determined by the small amounts of the element that could be safely and profitably used, bearing in mind the high specific activity. Apart from the radiation effects, which necessitate speedy analysis of the new compound immediately after its preparation, a major chemical problem is the rapid growth (0·5 per cent per day) of the lead daughter (^{206}Pb), so that a rapid and quantitative method of purifying the polonium before each experiment is required. Fortunately for the chemist, pure polonium metal can be obtained very easily, either by thermal decomposition of the very insoluble sulphide or by electrodeposition on to gold or platinum, followed by vacuum sublimation of the metal in Pyrex apparatus.

For reactions with gaseous reagents such as halogens, oxygen, and carbon monoxide, the metal is sublimed under vacuum into an X-ray capillary. The reaction takes place in this on admission of the appropriate gas. After re-evacuation, the

Table I *The principal compounds and reactions of polonium*


$PoCl_2Br_2$ Salmon pink
Br_2
$PoCl_2$ Ruby red Sub. 190° Orthorhombic?
H_2 at 200°
CO or H_2S at 150°
SO_2 at 18°
0·5N HNO_3
NO_3 Po O Po O NO_3 NO_3 White; dimeric?
100°
O=Po O Po O NO_3 Yellowish white; dimeric?
$Po(NO_3)_4.N_2O_4$ White (unstable)
Liquid N_2O_4
Liquid N_2O_4
130°
NO_2+O_2
Aq. HNO_3
Vacuum evaporation
Colourless solution; some anionic species present
Aq. HIO_3/HNO_3
$PoCl_4$ Yellow M.P. 300° B.P. 390° Monoclinic?
HCl (gas)
O_2 at 300°
PoO_2 F.C.C.⇌Tetragonal Yellow Red Sub. 885°/O_2 (760 mm)
$Po(IO_3)_4$? White Decomp. 350°
Aq. HCl
NH_4Cl at 100°
Cl_2 at 200°
O_2 at 250°
H_2 at 200° or vacuum at 500°
O_2
$PoCl_6^{--}$ Yellow solution
$(NH_4)_2PoCl_6$ Yellow F.C.C.
Po M.P. 254° B.P. 962° Simple 54° Simple cubic ⇌ rhombo- (α) 18° hedral (β)
SO_3 or conc. H_2SO_4
$SPoO_3$ Red Unstable
PoO Black
Conc. H_2SeO_4
$SePoO_3$ Red Unstable
Metals at 300–400°
Polonides Grey or grey-black
Aq. CsCl
H_2S
Cs_2PoCl_6 Greenish yellow F.C.C.
PoS Black
Vacuum at 275°
I_2 at 40°, 1 mm
Dilute aq. alkali
F_2
Br_2 at 250°
Aq. HI
$PoO(OH)_2$? Pale yellow
PoI_4 Black Sub. 200° (decomp.)
PoF_6 (gas) Only formed when long-lived polonium isotopes are used.
$PoBr_4$ Carmine M.P. 330° B.P. 360°/200 mm F.C.C.?
NH_4Br at 100°
$(NH_4)_2PoBr_6$ Red F.C.C. (explodes on heating)
Excess aq. HI
H_2S
Aq. HBr
Cs_2PoI_6 Black F.C.C.
Aq. CsI
PoI_5^-, PoI_6^{--} Red-brown (20°) or green (0°) solution
$PoBr_2$ Purple-brown Sub. 110°/30 μ
$PoBr_6^{--}$ Red solution
Aq. CsBr
Cs_2PoBr_6 Red F.C.C.
Aq. H_2SO_4 (<0·25N)
Aq. H_2SO_4 (>0·5N)
Aq. H_2SeO_4
Aq. CrO_3
Aq. H_3PO_4
$2PoO_2.SO_3$ White⇌yellow 250° Decomp. 550°
$Po(SO_4)_2.xH_2O$ White
$2PoO_2.SeO_3$ White⇌yellow 250° Decomp. >400°
$Po(CrO_4)_2$? Orange-yellow
$2PoO_2.H_3PO_4$ White
100° $-H_2O$
H_2O
$Po(SO_4)_2$ Purple Decomp. 550°
$2PoO_2.CrO_3$ Yellow-brown
ABBREVIATIONS
F.C.C. Face-centred cubic
Aq. Aqueous
Sub. Sublimes
Decomp. Decomposes

product can be analysed or made to react with a second gas, and so on. Insoluble compounds, precipitated from aqueous solution, cannot usually be separated from the mother liquor by centrifugation in a capillary because the precipitate is rapidly disrupted by the gases produced by the radiolysis of the solvent trapped in it. A microfilter stick must, therefore, be used for the separation [9]. The analyses of polonium compounds on the 200 microgram scale are carried out by means of conventional semi-micro techniques.

The chemistry of polonium

The principal compounds of polonium and some of the ways in which they are formed are shown in Table I. It can be seen that the chemistry of the element itself follows that of tellurium very closely, the most marked resemblance being shown in the reactions of the metal with sulphur trioxide (or concentrated sulphuric acid) and with concentrated selenic acid. These reactions give red, unstable solids, probably $SPoO_3$ and $SePoO_2$, both of which decompose to the unstable black polonium monoxide. The metal also forms polonides when heated with a wide variety of metals; most of these polonides are isomorphous with the corresponding tellurides [10]. On the other hand, the physical properties of polonium metal resemble those of thallium, lead, and bismuth, its neighbours in the Periodic Table, rather than those of tellurium.

The quadrivalent polonium halides, prepared from the elements or by the reaction of the dioxide with hydrogen halide, closely resemble their tellurium analogues, being brightly coloured, volatile, readily hydrolysed covalent solids. They give rise to complex acids in halogen acid solutions, from which insoluble salts of the larger cations, such as caesium and tetraethyl-ammonium, are readily precipitated. Polonium dichloride and dibromide appear to be more stable than the corresponding tellurium compounds and are easily prepared by reaction of the tetrahalide with reducing gases, such as hydrogen or hydrogen sulphide, at moderate temperatures.

The most marked differences from tellurium are shown in the salts formed by oxyacids, where polonium exhibits a more metallic character than tellurium, forming a disulphate, a tetranitrate, a phosphate, and a number of salts of weak acids, such as oxalic and acetic, that have no tellurium counterparts; polonium dioxide is also much less acidic than tellurium dioxide. The corresponding basic salts formed by polonium are, however, very similar to their tellurium analogues in composition and behaviour. The formation of quadrivalent polonium chromate is indicative of the difficulty of oxidizing the element to the sexavalent state. Indeed, the only reasonably certain example of this state is the volatile hexafluoride. This is prepared from the elements, but using the longer-lived polonium isotope ^{208}Po (half-life 2·93 yrs) [11].

This account of the chemistry of polonium is necessarily more brief than that to be found in the more comprehensive reviews [4–6, 12], but the chemistry, in so far as it is known, agrees well with that to be expected from the position of the element in the Periodic Table.

Practical applications

The principal use of polonium-210 is in the production of neutron sources, where the low γ-emission and the cheapness of polonium offset the rather short half-life. The neutron emission results from nuclear reactions of the alpha particles with nuclei for which (α,n) reactions are highly probable, such as beryllium, with which the polonium is mixed or alloyed for this purpose. Nuclear reactions of this type can also be used for the analysis of trace elements which cannot be determined by neutron activation, such as in the microdetermination of fluorine, where the radiation from sodium-22, formed by the reaction $^{19}F\ (\alpha,n)\ ^{22}Na$, can be counted quite easily. In the chemical field, polonium-210 has been used extensively in studies of the effects of alpha radiation on solids and liquids, while the isotope has found some application in industry in alpha-particle transmission gauges for thickness measurements in paper research, since the amount of energy lost by the alpha particle on passing through a given type of paper depends on the thickness.

Polonium has also been used in devices for eliminating static charges. The effect depends on the ionization by the emitted alpha particles of the air around the source. However, beta emitters are more commonly used for this purpose and are less dangerous.

The use in space satellites has already been mentioned. These satellites require a light-weight generator giving a constant output of electrical energy. The direct conversion of heat to electricity, using a radioisotope as the heat source, is particularly attractive, as no moving parts need be involved. The usual method of achieving the direct conversion is to use lead telluride or cobalt silicide thermoelectric elements, with the hot junction the container of the radioactive material and the cold junction an outer aluminium can thermally insulated from the inner container. The principle is similar to that of the conventional thermocouple. A constant output is achieved by allowing part of the heat to radiate away initially through a heat shutter; this gradually closes as the isotope decays, so that the temperature of the hot junction is kept reasonably constant. These converters require such large quantities of radioactivity that the method is suitable only for medium-power systems up to about 1 kilowatt.

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Lichens

Kenneth A. Kershaw

The unique nature of the lichens, in which what appears to be a single organism is actually an alga and a fungus growing symbiotically in a single thallus, was realized during the nineteenth century. However, little research was done until quite recently. This article describes attempts to cultivate the two symbionts separately, and it also discusses the distribution and ecology of the lichens.

The term 'lichen' appears to originate from the work of Theophrastus, who used it in his 'History of Plants' to describe superficial growths on the bark of olive trees. The term was kept in use by the early botanists, who applied it indiscriminately to thallose liverworts, such as *Marchantia*, as well as to lichens. This application was of course based on nothing more than general appearance. The true nature of lichens was not fully realized until 1867, when S. Schwendener published his 'dual-hypothesis' of the structure of lichens [13]. This stimulated an interest in the group that has been maintained to the present day. A lichen is a unique combination of a symbiotic alga and fungus; it has been surprisingly little studied in recent years. In particular, the fundamental problems concerning the inter-relationships of two plants in a composite thallus are almost completely untouched.

Culture experiments

Numerous attempts have been made to isolate the two symbionts of a lichen thallus. In general, little difficulty is found in culturing the alga, which always belongs to a common and widespread free-living genus, such as *Gloeocapsa*, *Nostoc*, *Stigonema*, or *Protococcus*. On the other hand, the fungus, although initially establishing itself in culture, often fails to develop a vigorous mycelium, and no report of the production of reproductive bodies under controlled conditions has appeared in the literature. V. Ahmadjian, for example, attempted to culture the spores or hyphae from 26 lichen species [1]. Of these, results with eight species were completely unsuccessful, and ten others were extremely slow to germinate and produced only small colonies (1–2 mm diameter after 9 months). The remaining species germinated and grew well, but no signs of production of conidia or formation of an ascus was found. Synthesis of a lichen from separate cultures of the symbionts has also been frequently attempted, and successful combinations of the alga and fungus, producing recognizable thalli, have been claimed. However, all these claims are based on sketchy evidence, and the experiments have never been successfully repeated. Many experiments have shown an initial close relationship between the two symbionts, the fungal hyphae closely clasping algal cells, but most cultures have never developed past this stage. E. A. Thomas [2] and V. Ahmadjian [3], using *Cladonia pyxidata* and *Acarospora fuscata* respectively, obtained a further development of this 'loose association' stage with a 'pseudoparenchyma' of fungal hyphae surrounding an 'algal layer'. Thomas actually records the formation of a thallus (unfortunately during his absence), but a further experiment involving 800 replicates failed to produce any podetia. G. D. Scott used discs of *Peltigera praetextata* (Flk). Vain. for similar experiments. He found that small finger-like growths (isidia) were formed along the cut margins of the disks [4]. The formation of isidia, he pointed out, is dependent on strict control of light intensity and humidity, and also on a reduction of nutrient concentration.

The available evidence seems to show that the initial combination of the symbionts is completely dependent on semi-starvation. If there are sufficient nutrients, either the fungus or the alga or both will show prolific but separate saprophytic growth. After the initial synthesis has been established, further development of the thallus may well depend on a more exact imitation of the natural environment. In nature, lichens are subjected to frequent drying out followed by periods of high humidity, and it is possible that this alternation of wet and dry conditions is essential in maintaining what appears to be a delicate balance between the two symbionts.

Physiology

Lichens are able to resist greater extremes of temperature and desiccation than any other group of plants, and this ability has led to the intriguing suggestion that any plant life that might be on Mars might well be lichen in character. O. L. Lange (1953) showed [5] that lichens could tolerate temperatures up to as high as 101°C (*Cladonia pyxidata* (L.) Hoffm.). Similarly, lichens can survive for up to 56 weeks of drought without any apparent signs of damage. This ability to withstand drought may be associated with the medulla of the lichen—it is suggested that this acts as a primitive water reservoir for the metabolically more active algal layer [6].

Lichens are able to absorb water either as liquid or as vapour. The absorption takes place over the whole surface of the thallus, and complete saturation is reached from an air-dry state in a matter of minutes. Similarly nutrients, both organic and inorganic, are absorbed in large amounts very rapidly, and again the absorption takes place over the entire thallus surface. Protein synthesis and rate of breakdown appear to be slow, and this, together with the high absorption of nutrient and water, explains to some extent at least the ability of lichens to withstand periods of extreme desiccation. Furthermore, the slow growth of most lichens (see below) correlates with this low rate of protein synthesis.

The carbohydrate metabolism of lichens has received little more than general treatment until recently, when D. C. Smith, using ^{14}C as a label, demonstrated the importance of mannitol in the carbohydrate syntheses of *Peltigera polydactyla* (Neck.) Harm. [6]. Disks of lichen thallus were floated in daylight on sodium bicarbonate solution labelled with ^{14}C and the extracts analysed by chromatography. A large proportion of the ^{14}C fixed in photosynthesis initially appeared in mannitol, and similar experiments using labelled glucose showed a rapid conversion of the glucose into mannitol. The site of formation of the carbohydrates has been assumed to be in the algal layer, and Smith gives data that confirm this. Disks that had been illuminated were immersed in a labelled sodium bicarbonate solution; they were then kept in the dark and sample disks

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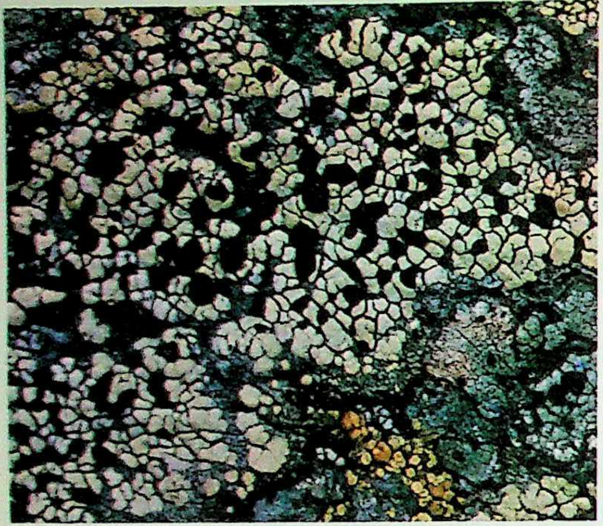
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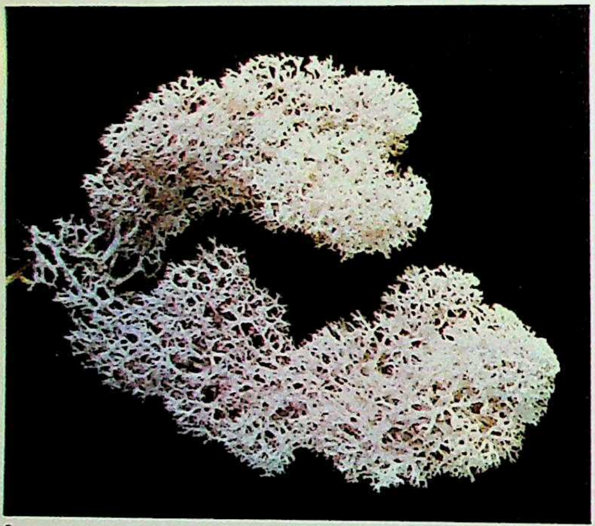
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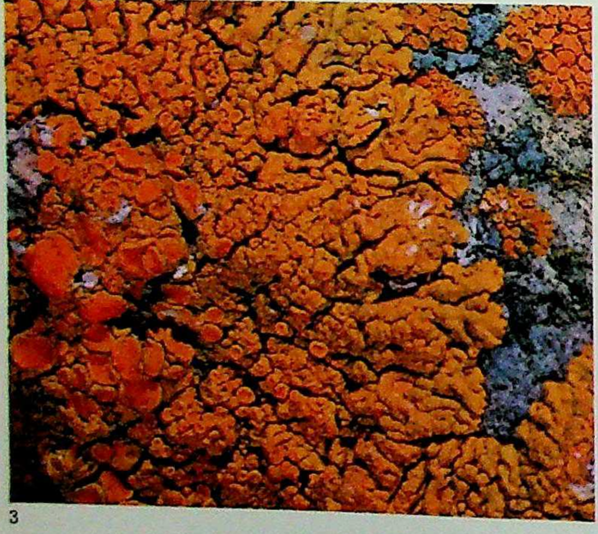
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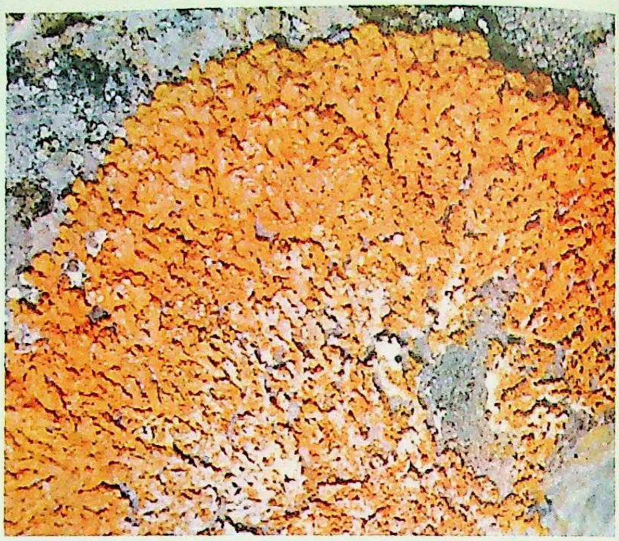
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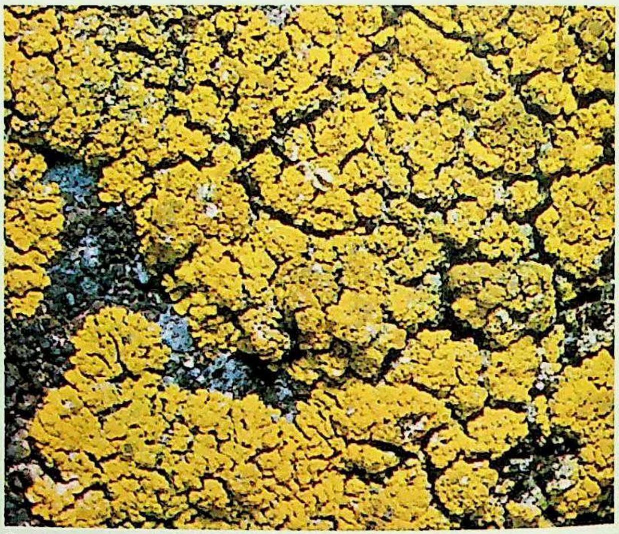
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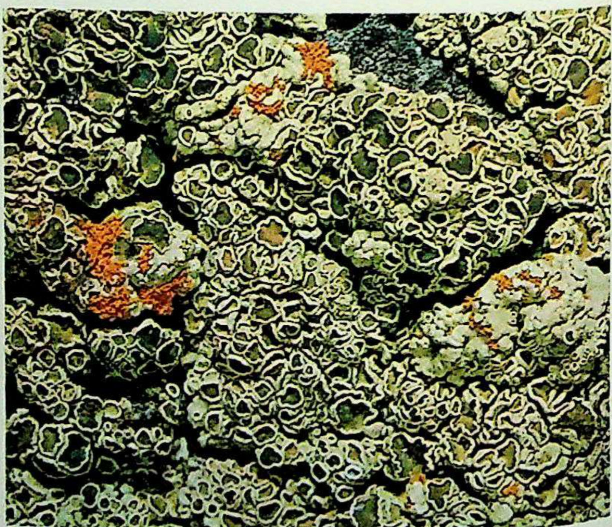
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Figure 1 Rhizocarpon alpicola *(Hepp.) Rabenh.* (× 2·8)

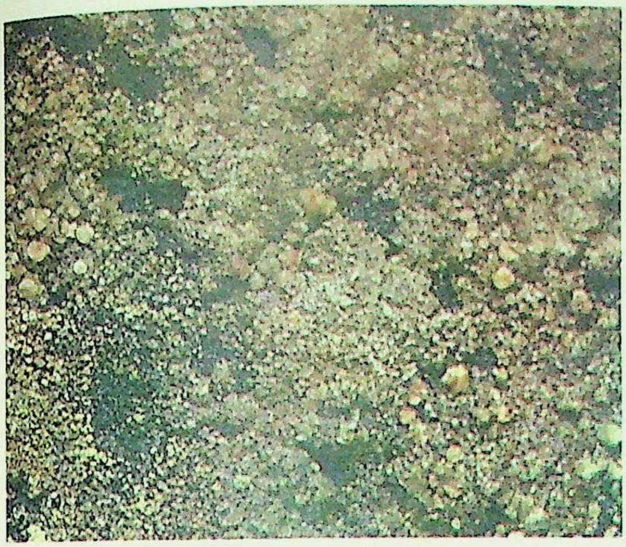
Figure 2 Cladonia alpestris *(L.) Rabenh.* (× ½)

Figure 3 Caloplaca elegans *(Link.) Th. Fr.* (× 2·8)

Figure 4 Caloplaca verruculifera *(Vain.) Zahlbr.* (× 2·8)

Figure 5 Candelariella crenulata *(Wahlenb.) Zahlbr.* (× 2·8)

Figure 6 Lecanora melanophthalma *(Ram.) Ram.* (× 2)



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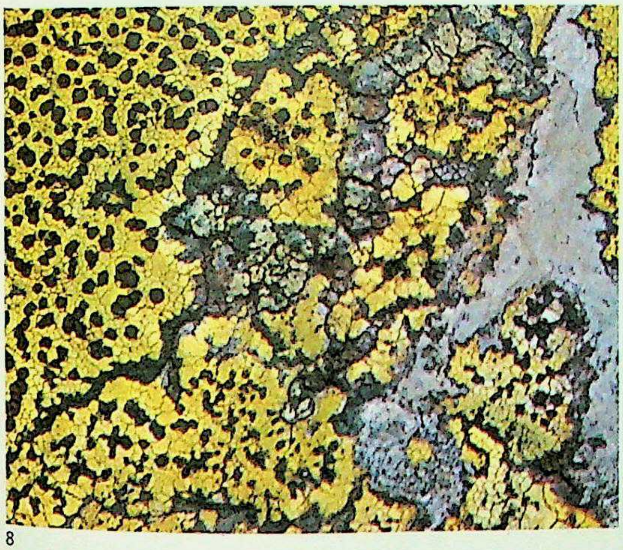

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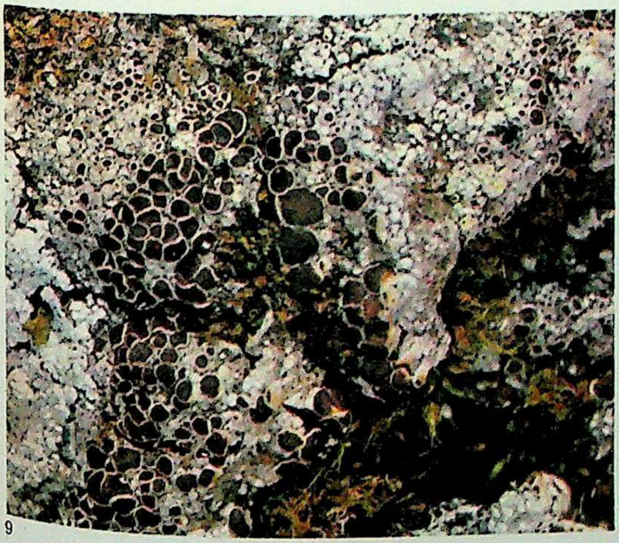

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Figure 7 Lecanora conizaeoides *Cromb.* (×2·8)

Figure 8 Rhizocarpon geographicum *agg.* (×2·8)

Figure 9 Lecanora epibryon *Ach.* (×2·8)

were removed at regular intervals. The amount of ^{14}C present in the medulla and algal layers was then estimated; the results are given in figure 10. The transfer of the products of photosynthesis took approximately two hours and continued for some five hours after the light source had been removed. It would thus appear that the medulla might function as a storage tissue for carbohydrate products. However, in order to confirm this it would be necessary to show that such products were released from the algal zone. This evidence is as yet not available.

Ecology

The distribution of all epiphytes on the trunks of trees varies markedly around the trunk, and this variation is shown extremely strongly by lichens. The microclimatic gradients that undoubtedly exist usually limit lichen populations to the north side of a trunk, in the Northern Hemisphere, unless the general average humidity is constantly very high. Even then, there is a marked difference in their abundance. Lichens similarly show very marked preferences for particular types of rock. Limestone has an extremely characteristic flora, with the genus *Caloplaca* predominant. This is quite different from that of siliceous rocks, which are characteristically colonized by the genera *Lecidea* and *Rhizocarpon*, although both these genera contain species, such as *Lecidea immersa* Ach. and *Rhizocarpon calcareum* (Weis.) Th. Fr., that are restricted to basic rocks. There is a similar, but even more marked, preference shown by some lichens for a nitrogen-rich habitat. Such species occur abundantly near the nesting or perching sites of birds, or close to farm buildings. These nitrophilous species have a very restricted distribution in other habitats, and in the arctic they are completely absent from areas not receiving any regular supply of animal excreta. In arctic and sub-arctic areas, nesting or perching sites are readily identified solely from the associated lichen flora. This is characteristically dominated by *Caloplaca elegans* (Link). Th. Fr. (figure 3), *C. verruculifera* (Vain.)Zahlbr. (figure 4), *Candelariella vitellina* (Ehrh.) Müll. Arg., *C. crenulata* (Wahlenb.) Zahlbr. (figure 5), *Lecanora melanophthalma* (Ram.) Ram. (figure 6), and *L. thulensis* Th. Fr. Apart from this recognition of the general preferences of lichen species for basic and acid rocks, little work has been done on the ecology of lichens. Even the marked maritime zonation of lichens has not received any detailed study.

One unusual aspect of lichen ecology that is becoming increasingly evident is the extreme susceptibility of lichens to air pollution. This is possibly due to the indiscriminate and rapid absorption of solutes over the surface of the thallus [6]. The visible manifestation of the sensitivity to atmospheric pollution is the virtual absence of lichens from towns and industrial areas in general. E. Skye investigated the lichen flora in the area surrounding a shale-oil works at Kvarntorp in Sweden, and concluded that the distribution corresponded markedly with the levels of air pollution, mainly by SO_2 [7]. The lichen scarcity in built-up areas may, however, equally well reflect the low humidity of these areas. The drainage system of a city deals very efficiently and quickly with rainfall that would otherwise evaporate at a slow rate and it thus lowers to some extent at least the general level of atmospheric humidity. It seems most probable that both factors interact, but the scarcity of lichens in wide areas surrounding towns and cities would suggest pollution to be the over-riding factor.

There are a few lichens that are tolerant of pollution, and these occur abundantly in industrial and suburban areas. *Lecanora conizaeoides* Cromb. (figure 7) is a notable example, and its distribution in this country appears to be governed by

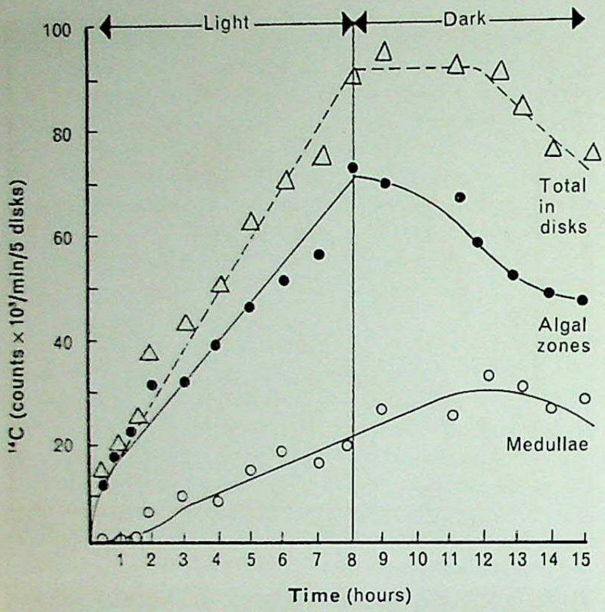
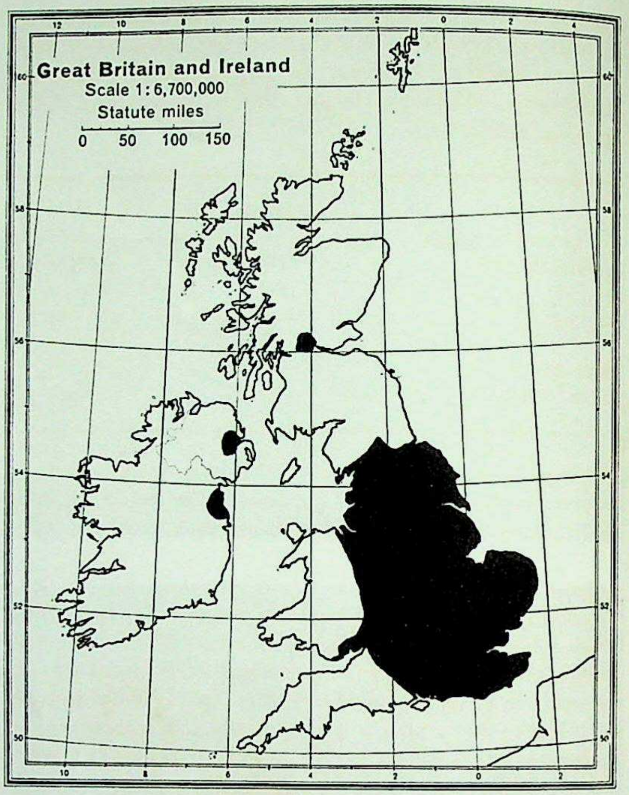


Figure 10 *Distribution between the algal zones and medulla of* Peltigera *disks of substances labelled with* ^{14}C *in photosynthesis [6].*

the level of pollution (figure 11). Thus it is rare or virtually absent from large areas of S.W. England, Wales, N.W. and W. Scotland, and most of Ireland, while small areas occur near large cities such as Glasgow, Edinburgh, and Dublin. This species seems to be an early colonizer of trees and brickwork and to be unable to withstand competition from other lichen species. It is in fact replaced by other closely related species in areas with little or no pollution. A similar case is found in *Stereocaulon pileatum* Ach., which is a montane and sub-montane species fairly frequent in the west of the British Isles. Again it seems to be an early colonizer of rock surfaces and is commonly found in abundance on stone walls and spoil heaps near, for example, old iron-workings (figure 12). In 1960 a surprising record turned up from a suburban brick wall in S.E. England, and since then numerous gatherings have been made in the London area (figure 12). It would seem that this species is typically an early colonizer and incapable of withstanding competition. However, being tolerant of air pollution, it has extended its range and is now becoming a frequent colonizer in suburban London, where few other lichens can exist. The frequency of these recent records from the London area reflects the density of lichenologist population rather than any special climatological factor of the area, and it seems probable that records will eventually turn up from other large cities.

F. H. Brightman discusses [8] the apparent preference of lichens for asbestos roofing in polluted areas, and relates this to the high water-absorbing power of the substratum and the high base content, with the consequent power of neutralizing acidic atmospheric pollutants. The data were obtained from an asbestos-tiled roof which was re-tiled in 1957 and thus offered an ideal opportunity to examine in detail the flora of a large number of the tiles. Four species were present, *Squamaria muralis* (Schreb.) Elenk., *Lecanora dispersa* (Pers.) Röhl, *Rinodina demissa* (Koerb.) Arn., and *Candelariella vitellina* (Ehrh.) Müll.-Arg. The density of *Squamaria* rosettes was approximately one per square metre, with diameters of up to 6 cm. This is remarkably high for a built-up area only eight miles from the centre of London, and with a high level of pollution. Similarly the density of the other species was extremely high—up to 368 apothecia



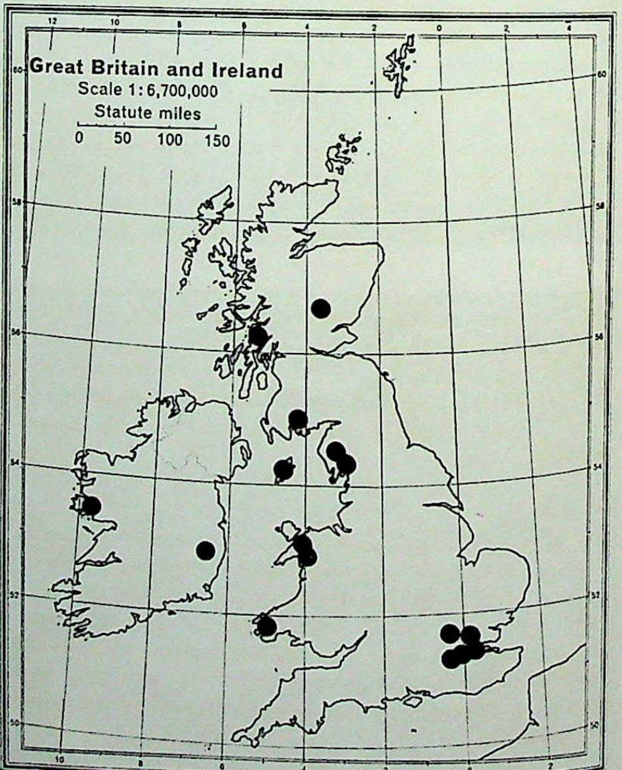


Figure 11 (top) *Approximate distribution of* Lecanora conizaeoides *in the British Isles, showing the areas where it is abundant (black) contrasting with lightly polluted areas, where it is rare or absent.*

Figure 12 *Distribution of records of* Stereocaulon pileatum *in the British Isles. Areas of abundance shown in black*

(fruiting bodies) per cm^2, being recorded for *Lecanora dispersa*. An adjacent clay-tiled roof of the same age, height, slope, and aspect was used for a comparison and was found to be completely devoid of lichens. The properties of the two types of tile are given below:

	Asbestos tile	Clay tile
Water absorption	12·2%	4·1%
pH	10·0	8·5
Nitrates	12 parts per 100 000	1 part per 100 000
Sulphates	7·0%	Nil
Bases (calculated as $CaCO_3$)	21·5%	0·6%

The figures clearly suggest that the high water-absorbing properties and the basicity of the asbestos are the factors most likely to produce the prolific lichen growth.

Growth

The slow rate of protein synthesis that was demonstrated [9] by Smith makes it reasonable to expect a generally slow rate of growth in lichens. E. Frey [14] examined in detail the growth rates of over 40 species, and found that the maximum growth-rates were of the order of 2–4 cm per annum in some species of *Peltigera* down to as little as 1–2 mm in the genus *Rhizocarpon* (*R. geographicum* agg., figure 8). This slow growth has been used in dating terminal glacial moraines. The maximum diameter of lichen thalli of a number of species from dated moraine surfaces are recorded, and a graph is then constructed that plots size of thallus against time. Surfaces of unknown age in the area can then be dated from the graph with a reasonable degree of accuracy. R. E. Beschel gives data for several species that show an initial sigmoid growth curve followed by a more or less continuous rise [10]. The growth curve for two of the species is given in figure 13. The genera *Rhizocarpon*, *Aspicilia*, and *Lecidea* have been found to be of most use in this context, and their largest thalli seem to be 600–1300 years old in the Alps and 1000–4500 years in W. Greenland. More recently, the statues on Easter Island were dated in a similar manner by G. Follman [11]. The dates agree fairly well with dates based on archaeological evidence. *Physcia picta* (Swans.) Nyl., *Diploschistes anactinus* (Nyl.) Zahlbr., and *Lecidea paschalis* Zahlbr. were used. The oldest statues were shown to be about 700 years old, but the average age of the various surfaces examined was only approximately 430 years.

General

Now that amino-acids and vitamins, for example, can be obtained in a high state of purity, it seems likely that the growth and reproduction of the fungal symbionts of many lichen species will be successfully studied under culture conditions. Similarly, the combination in culture of the two symbionts of a lichen will ultimately be achieved. This will open up a fresh approach to the many taxonomic and ecological problems that are outstanding.

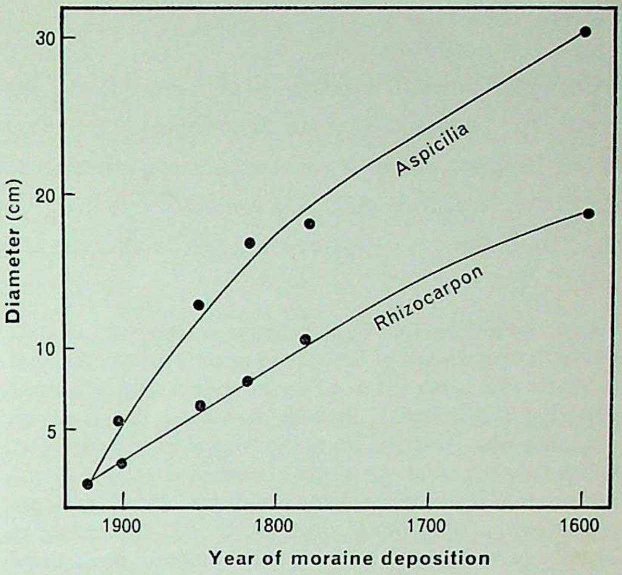


Figure 13 *Growth curves for* Aspicilia cinera *and* Rhizocarpon geographicum *growing on moraine detritus of known date [10].*

Several lichen acids have been shown to have antibiotic properties [15] and have been used with varying degrees of success on a range of bacteria. However, until lichens can be cultured on artificial media, there seems little commercial import in this field, unless substances with much more powerful antibiotic properties are discovered. On the ecological side, much remains to be done; the production of the epiphytic lichens that represent the staple food of reindeer during the winter months in British Columbia has been studied by R. Y. Edwards, J. Soos, and R. R. Ritcey [12], and it is clear that the possibilities of lichens as food or fodder should not be ignored.

Acknowledgment

I wish to thank Mr Tony Horne of this department for his photographic work in the illustration of this article.

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The International Geophysical Year in retrospect

Sir Harrie Massey

The International Geophysical Year (IGY) lasted officially from 1st July 1957 to 31st December 1958, but it was in preparation for at least two years before its official opening. It is estimated that at its height about 30 000 scientists, engineers, and technicians were working on the IGY programme, and the cost was probably some £500 000 000 per annum. Looking back six years after its conclusion, it is natural to ask what was achieved, and whether the results justified the effort.

Before considering the IGY in terms of tangible scientific results, it is important to notice some general aspects. There is no doubt that it has led to a very great expansion of interest and effort in geophysical research, so much so that one hears talk, with some justification, of the 'explosion in geophysics'. When the time came there was a marked reluctance to terminate, or even to run down, the world-wide, highly organized programme at the end of 1958. At the IGY conference in Moscow in August 1958 it was agreed to continue international co-operation less intensively throughout 1959; this period was known as IGC (International Geophysical Cooperation) 1959. In addition, arrangements were made by the International Council of Scientific Unions (ICSU) to establish two special committees to organize continued international cooperation in the three sections of the Geophysical Year that proved to be of particular novelty or importance. Two of these were the Committee on Space Research (COSPAR), and the Special Committee on Antarctic Research (SCAR). A third, the Special Committee on Oceanographic Research (SCOR) was already established in 1957.

Apart from these specific arrangements, there has been set up the International Committee on Geophysics (CIG) to coordinate research in geophysics carried out throughout the world under different auspices. All these subjects depend for their successful prosecution on far-reaching cooperation between scientists in different countries, and it is a very great advantage that this cooperation has been placed on such a firm basis. This in itself is one great gain resulting from the IGY—we shall see later what a remarkable degree of cooperation has been achieved in Antarctica.

Organization of the IGY

The IGY was organized in terms of three major sections. Broadly speaking, the first was concerned with the Earth's atmosphere and solar–terrestrial relationships; the second with surface phenomena on the Earth; and the third with the internal structure of the Earth.

The Sun is a variable star exhibiting disturbances such as sun spots, the scale and frequency of which follow an 11-year cycle. Atmospheric effects due to solar disturbances are much more frequent and prominent around a maximum in the disturbance cycle. It was for this reason that the IGY was chosen to cover the period 1957–58, when a sunspot maximum was expected. It proved a very fortunate choice, for 1957 yielded the highest yearly mean sunspot number since records began in 1778 (figure 1).

A further good augury was the fact that the Year was ushered in by a strong solar disturbance on 28th June 1957. So many data have been obtained around a period of maximum disturbance that for comparison it is desirable to obtain similar information during a period in which solar disturbance is at a minimum. An International Year of the Quiet Sun (IQSY) is therefore being organized by the CIG for the period 1964–65. This should be a valuable supplement for the IGY; the programme is described in the editorial on page 54 of this issue of ENDEAVOUR.

The detailed organization of the IGY was in terms of seventeen disciplines. Solar activity, meteorology, ionosphere, geomagnetism, aurora and air glow, cosmic rays and nuclear radiation, were within the atmosphere and solar–terrestrial relations section. Oceanography, glaciology, and precision measurement of latitude and longitude were within the section dealing with the Earth's surfaces. Seismology and gravity measurements were in the section concerned with the Earth's interior. In addition, two further sections overlapped with a number of the disciplines. One dealt with observations made from rockets and satellites, the other with observations carried out in Antarctica. These represented big new possibilities for geophysical observation not previously available to any extent. The decision to group methods on these two lines into separate sections proved very sound, and it led to very rapid developments in both directions; the two activities have now become part of normal geophysical practice.

The solar patrol

Turning now to specific results and achievements, we can begin by discussing the organization of the solar patrol. As indicated earlier, the Sun exerts a dominant influence on the behaviour of the Earth's atmosphere through the interaction of its electromagnetic and particle radiation with atmospheric constituents. When the Sun is disturbed, its emission of certain short-wave radiation is enhanced. This is usually even more marked for the particle radiations, which are relatively weak under quiet conditions. Solar disturbances are often indicated by the appearance of a bright emission region for visible light, known as a solar flare, an example of which is illustrated in figure 3.

Effects due to electromagnetic radiation may be distinguished by their simultaneous appearance over the sunlit face of the Earth within minutes of the occurrence of the related solar flare. They include radio fade-outs, enhanced intensity of atmospherics and magnetic variations of a type known as magnetic crotchets.

The particles from the Sun are electrically charged, so that their motion is affected by the Earth's magnetic field; in consequence, the terrestrial effects show a strong dependence on latitude, being concentrated towards high latitudes. Some of the events due to particles—such as enhanced solar cosmic-ray reception and radio black-out over the polar cap (polar cap absorption)—begin within an hour of the associated solar

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Was born in 1908 and was educated at the University High School, Melbourne, and Melbourne University. After graduation he undertook research work in atomic physics at the Cavendish Laboratory, Cambridge. In 1933 he was appointed head of the department of mathematical physics at Queen's University, Belfast, and in 1938 became Goldsmid professor of mathematics at University College, London. He held this chair until 1950, when he became Quain professor and head of the department of physics at the same college. He is chairman of the British National Committee for Space Research.

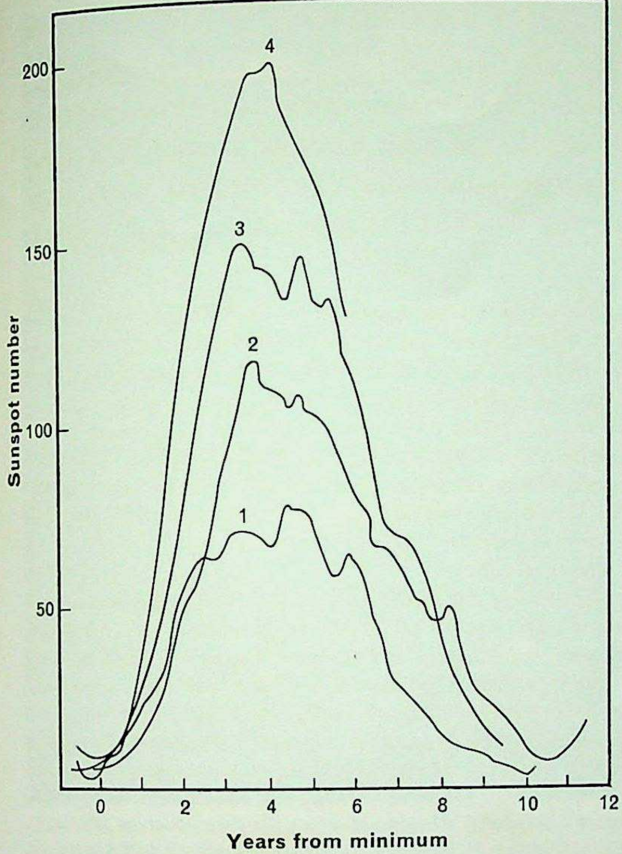


Figure 1 *Variation of sunspot number over the last four sunspot cycles: 1, 1923–33; 2, 1933–44; 3, 1944–54; 4, 1954–.*

flare. Others, such as magnetic and ionospheric storms and decreased intensity of cosmic-ray reception from the galaxy, begin after a time delay of many hours, up to 30 or 40 in some cases. Figure 2 illustrates the relation between the different events in terms of typical records.

The way in which all these events are produced from the disturbance on the Sun is very complex, and it is necessary to study in as great detail as possible the different aspects of related effects. For this purpose, it is important to develop a warning system, so that scientists in different countries can be informed of the imminent likelihood of a solar flare in time to prepare for observations of the consequent events.

During the IGY, 52 observatories in different parts of the world took part in the solar patrol; as an indication of the effort involved, the Royal Observatory at the Cape of Good Hope recorded 694 flares during nine and a half months. The Sun's activity was watched, at some stations, for nearly 90 per cent of the possible time.

Because of the warning system for solar disturbances, very much more complete information than hitherto about the terrestrial effects and their relation to the Sun was obtained on many occasions. One enterprise that yielded very useful results was carried out on an island off the Californian coast, using Nike-Cajun rockets which could be launched within minutes of receipt of a signal announcing the occurrence of a solar flare. These rockets contained equipment to measure the intensity of the Lyman α radiation (wavelength 1216 Å) and of X-radiation in different wavelength bands between 20 and 2 Å emitted by the Sun. Contrary to expectation, no appreciable increase of the Lyman α radiation was observed immediately after the flare. This is in marked contrast to the Hα line (6563 Å), the enhanced emission of which is responsible for the visible flare. In the X-ray region, it was found that the flare is accompanied by an increase in relative intensity of the shorter wavelengths. From these results, which have been confirmed in later flights, both in sounding rockets and in satellites, it appears that radio fade-outs are due not to enhanced ultraviolet emission but to the emission of quite short X-rays. These penetrate quite deeply into the atmosphere, to within 70 km of the Earth's surface, at which levels they produce increased ionization. Because of the comparatively high atmospheric density at 70 km compared with that in the main ionosphere, radio waves are absorbed rather than reflected by the low-lying ionized layer—hence the radio fade-out.

Use of sounding rockets

Many other examples of the effective use of rockets and satellites during the IGY can be cited. Both the United States and the Soviet Union carried out extensive programmes of research with sounding rockets, in which a wide variety of upper atmospheric phenomena was studied. For the first time, launching sites were spaced over a considerable range of latitudes. The United States, by arrangement with the Canadian Government, established a range in the Arctic at Fort Churchill and

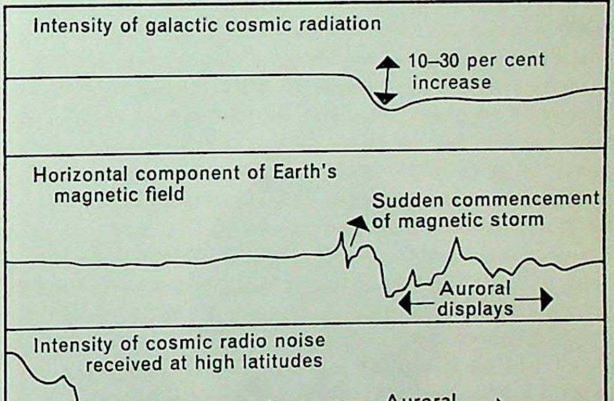
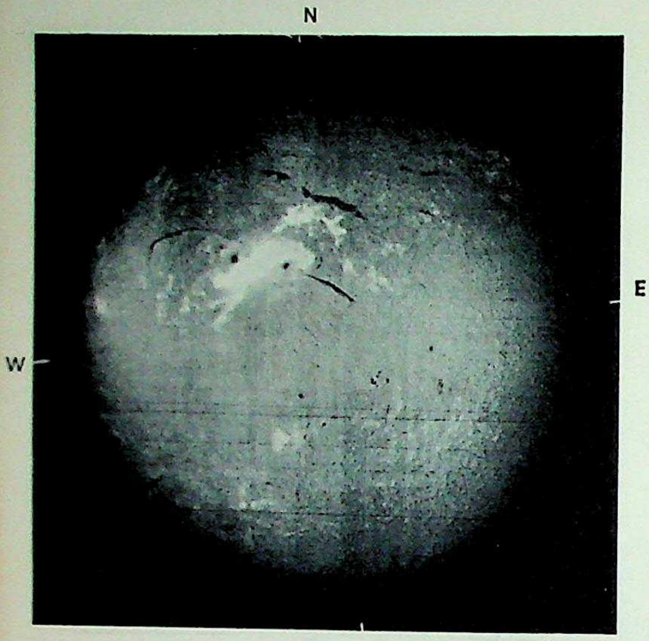
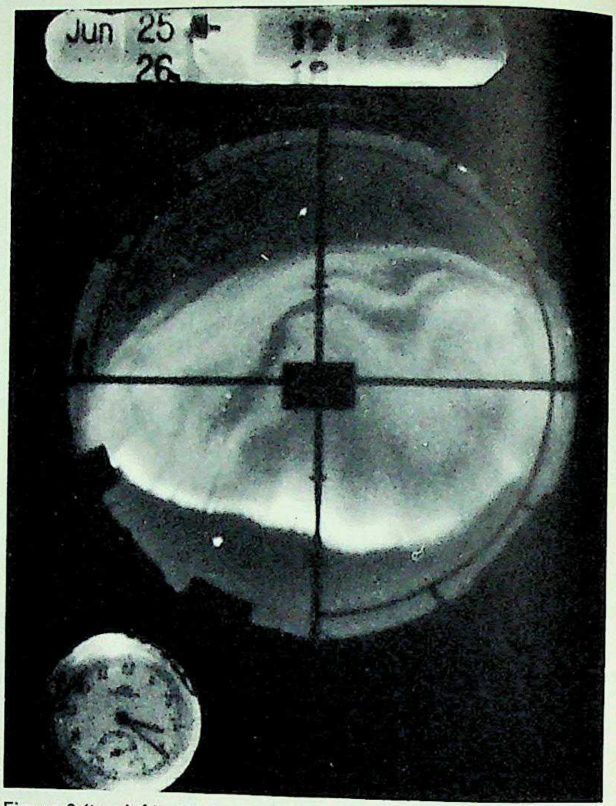
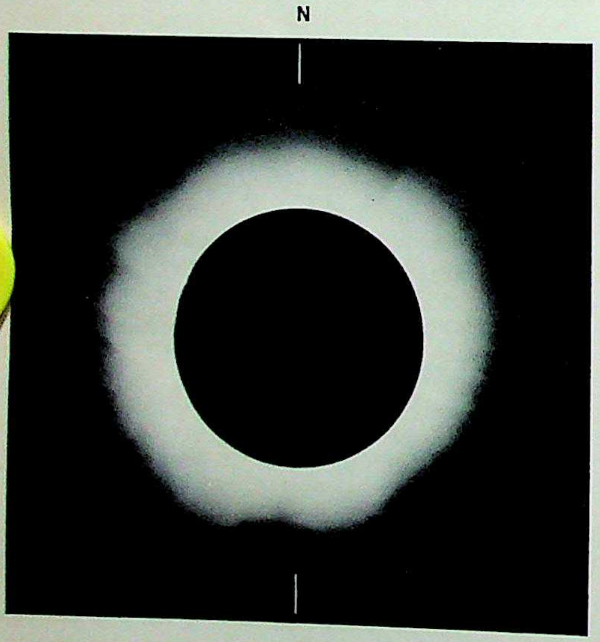


Figure 2 *Illustrating the variation of correlated solar and terrestrial quantities after a solar flare. The variations shown are schematic, though typical. Note the different time delays associated with the onset of the different phenomena.*







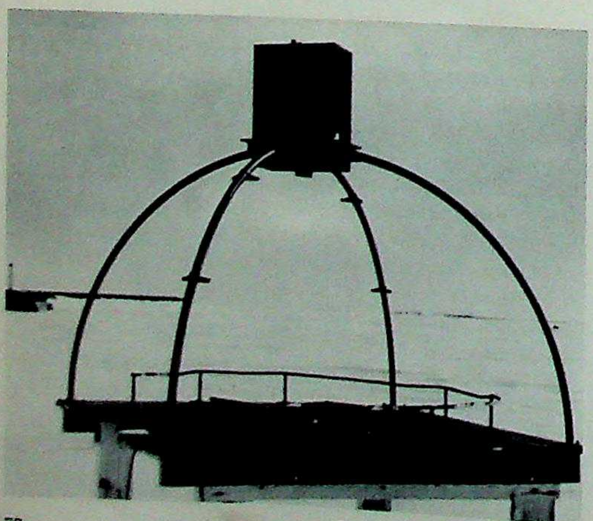


Figure 3 (top left) *Photograph of a solar flare observed 25th July 1946 at Meudon. (Photograph kindly supplied by Dr L. d'Azambuja).*

Figure 4 (centre left) *Photograph (kindly provided by the Royal Astronomical Society) taken during totality at the solar eclipse of 1905, showing the solar corona from which solar X-rays are emitted.*

Figure 5 (bottom, left). *An all-sky camera. The camera is mounted vertically above a convex mirror.*

Figure 6 (above). *An aurora photographed with an all-sky camera.*

also conducted a series of launchings of 'rockoons' from a ship as it sailed from California to Antarctica. A rockoon is a small rocket carried aloft by a balloon and launched from an altitude of about 15 miles. In this way the altitude range is much increased as, when the rocket is launched, it is already well above most of the atmosphere so far as frictional drag is concerned.

Among many interesting observations carried out in the rockoon programme, we may select the investigation of the equatorial electrojet. This is an electric current system that flows round the geomagnetic equator at a height of about 100 km. It covers a range only 10–20 km in height and about 300 km in width, and it is responsible for the strong magnetic field variations at equatorial latitudes. To observe the electrojet, sensitive magnetometers were taken through it in rockoons. Penetration into the current layer is indicated by a sudden change in slope of the variation of magnetic field with height. Figure 7 shows the variation of current density with height derived from magnetic field observations made from a flight over Fanning Island (3° 23′N, 158° 41′W).

On 12th October 1958, sounding rockets were used for the first time during a solar eclipse. Four such rockets were launched by U.S. scientists from the Danger Islands in the Pacific within the zone of totality. These rockets contained equipment to measure the intensity of both solar ultraviolet and X-rays.

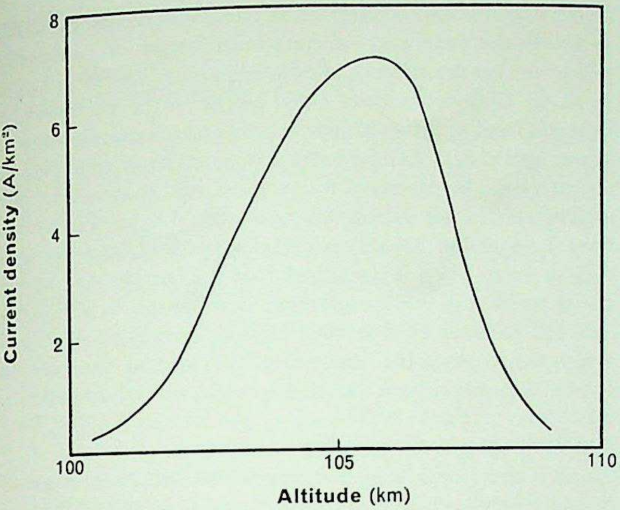


Figure 7 *Variation of electric-current density in the atmosphere with height above Fanning Island, observed in a rocket flight on 17th October 1957, showing the existence of the electrojet. (From* IGY Bulletin, *No. 25, 1959.)*

It was found that, whereas the ultraviolet radiation decreased in intensity during the eclipse, that of the X-rays remained unaltered. This shows that the X-rays are emitted from the solar corona, the tenuous solar atmosphere that is not obscured during an eclipse (figure 4).

The radiation belts

Undoubtedly the most remarkable discovery made during the IGY by means of satellites was that of the great radiation belts that surround the Earth. Radiation counters, designed to observe cosmic rays, were included in the equipment of most of the early satellites. Already in Sputnik II, which carried the dog Laika, the counter had indicated a considerably greater intensity than expected, but the short lifetime of the power supply in this satellite so limited the observing period that no definite conclusions could be drawn. The next evidence came from the counters included by J. A. van Allen in the first successfully launched American satellites, Explorer I and Explorer III.

In both cases it was found that the counters, while recording cosmic radiation as expected when at an altitude less than 700 km, periodically went out of action when the satellite reached greater distances. Van Allen attributed this to the presence, at the greater distances, of such a high intensity of particle radiation that the counters were choked. He confirmed by laboratory experiment that the instruments would indeed fail to respond if the counting rate exceeded that from cosmic rays by a factor of 10 000 or more. Finally, by including counters capable of recording such high rates in the next satellite, Explorer IV, van Allen confirmed the existence of the regions of high radiation intensity and produced evidence suggesting that the confines of the region are determined by the lines of force of the Earth's magnetic field.

Subsequent observations with the deep-space probes Pioneer III and Mechta have shown that two belts exist, and there is now general agreement that the Earth's magnetic field exerts a major control on the geometry of the regions (figure 8). The importance of the belts for solar–terrestrial relations is certainly very great, and their discovery represents a major step forward.

Analysis of satellite orbits

Another direction in which extraordinarily rapid progress was

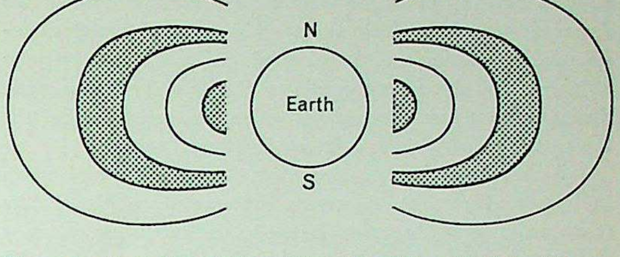


Figure 8 *Illustration of the relationship of the radiation belts (shown shaded) to the Earth's magnetic field, lines of force of which are shown. The outer belt is very variable in extent, and the situation illustrated is appropriate to quiet solar conditions.*

made soon after the first satellite launchings was in the determination of the figure of the Earth from observations of satellite orbits. It was soon found that the determination of equatorial flattening—defined as $(a-b)/a$, where a and b are respectively equatorial and polar diameters—from gravity surveys was not as accurate as was believed. The pre-satellite figure was $1/297{\cdot}10 \pm 0{\cdot}4$, while that derived from satellite orbit analysis is $1/298{\cdot}24 \pm 0{\cdot}02$.

It is also possible to derive a great deal of information about the air density at the perigee height of an earth satellite from observation of the rate of decrease in the period of revolution. This subject was taken up with enthusiasm during the IGY and has shown that, at altitudes above 200 km, the air density is much more variable than at lower altitudes and shows unmistakable evidence of a correlation with the occurrence of solar disturbances. Analysis of satellite orbits continues intensively, and is still yielding fresh and more precise information.

Antarctic research

Great interest attaches to the use of the Antarctic continent as a base for geophysical research of all kinds. As remarked earlier, the geomagnetic field exerts a profound influence on many atmospheric phenomena. This field is strongest at the geomagnetic poles, so that the geomagnetic control is more apparent over both the Arctic and Antarctic regions. In both cases ionospheric observations are assisted by the almost complete absence of man-made electrical interference. Although geophysical stations had been located in the Arctic for some time, little of a systematic character had been done in the Antarctic.

In order to correlate ionospheric and other geomagnetically affected atmospheric phenomena, over the two polar regions, it was most desirable to develop synoptic observations over the southern region. Important as this is, there are many other reasons why the establishment of Antarctic observer stations is important. For example, the weather and climate over vast areas of the southern hemisphere are strongly influenced by the Antarctic ice-cap. It is therefore most important to understand the atmospheric circulation, temperature distribution, and other aspects of Antarctic meteorology. As the Antarctic ice-cover is nearly 90 per cent of that over the whole globe, it is clear that a unique situation exists for the study of glaciology, including not only present-day conditions but the history and prehistory of the ice-cap, on which we could base more reliable ideas about the variations of the Earth's climate through the ages than we have at present.

During the IGY, the opportunity for commencing a thorough geophysical study of Antarctica was seized with enthusiasm. Twelve nations—the Argentine, Australia, Belgium, Chile, France, Japan, New Zealand, Norway, South Africa, the Soviet Union, the United Kingdom, and the United States—set up or maintained as many as 57 stations in south polar regions, over 40 of which were on the mainland or in the Antarctic peninsula. Data on a wide range of upper atmospheric, meteorological, glaciological, and gravity surveys were obtained, and these were supplemented by observations made during the overland traverses, of which the most extensive was the Commonwealth Trans-Antarctic Expedition.

It is not possible here to select more than one or two examples to illustrate the scope and nature of the results obtained. The south polar ionosphere was found to exhibit properties very different from those encountered at low latitudes. Thus the maximum electron concentration in the F_2 (uppermost) layer of the ionosphere over Halley Bay, the Royal Society base in Antarctica, at noon in the winter was found to be greater than the corresponding maximum at noon in the summer. At first sight, this is most surprising, because during the winter at this latitude the F_2 layer is not illuminated by the Sun at any time of the day. We must suppose that the winter F_2 region is maintained through ionospheric movement, as direct maintenance by the ionizing action of solar electromagnetic radiation is excluded. Effects due to ionization by solar corpuscular streams, which are pronounced in polar regions, must also contribute.

The aurora was extensively studied during this time, and a very large number of photographs were taken with the all-sky camera (figures 5 and 6). A correlation between auroral phenomena in the Arctic and Antarctic was obtained, as well as some remarkable results, due particularly to Russian scientists, which suggest that the particles entering the polar caps during solar disturbances are precipitated in spiral paths.

Antarctic meteorology exhibits extreme conditions in many directions—storms of hurricane intensity, areas of persistent low pressure, and great extremes of temperature. One astonishing phenomenon which was observed in some detail is the so-called explosive warming which occurs during October in the Antarctic stratosphere at a height of about 20 km. Over eight months the stratosphere cools down, from −32°C in mid-November to −88°C in early August. The four months' warming period which occurs during spring is in fact largely confined to October. Thus at the South Pole station manned by scientists from the United States the temperature maximum was reached in late October and early November, representing a total increase of temperature of 60°C in less than 3 months, 80 per cent of the rise occurring in October.

A great deal of seismic sounding was carried out to determine the thickness of the south polar ice-cap, and it was found that the total ice cover is over 40 per cent greater than previously thought. Ice thicknesses as great as 4700 m were observed in some localities. Considerable attention was paid to the problem of deciding whether the ice-cap covers a single continent, a divided continent, or a number of islands: the answer is still not definite. Among other interesting evidence bearing on the problem we note the determination of the thickness of the Earth's crust under the south polar ice-cap which was made from observations, at three Antarctic stations, of the times of arrival of disturbances propagated from centres in the Indian Ocean. As pointed out by the New Zealand scientists F. F. Evison, C. E. Ingham, R. H. Orr, and J. H. Le Fort, the crustal thickness obtained (35 km) was consistent with that for the continents (30–40 km), but not with that for the oceans (5–15 km).

The Antarctic Treaty

The overwhelming success of the IGY expeditions encouraged the various participating scientists to plan for indefinite continuation of the work. This has been achieved through the Antarctic Treaty, according to which the signatory countries, whose scientists had cooperated so effectively during the IGY, agreed to the reservation of Antarctica for peaceful uses only and to the continuation of international scientific co-operation there. In addition, nuclear explosions were prohibited and a system of free inspection of any part of Antarctica was instituted. It was agreed also that the status quo on all national territorial claims should be preserved for 30 years, and that no scientific activity carried out during this period could be used as a basis for a later claim. All this is quite exceptional, and becomes even more so when it is realized that the carrying out of the co-operative scientific programme is entrusted to the International Council of Scientific Unions, a non-governmental association of scientific academies. This is done through the Special Committee for Antarctic Research, which is most active.

Oceanography

Another direction in which the IGY marked a new phase of intensive activity is that of physical oceanography; hitherto a rather neglected subject, it developed very rapidly during 1957–58. No fewer than 80 ships from 20 countries took part in ocean surveys. The introduction of new techniques provided new information not previously accessible. In particular, the neutrally buoyant acoustic float developed by J. C. Swallow just before the IGY has made it possible to measure ocean currents at depths far below the surface. Thus it was found that, while in the Gulf Stream off North Carolina, there was a strong northerly current, at about 3000 m depth a counter-current flowing at 0·3 knot was observed. Again, in the upper 1000 m of the Equatorial Pacific Ocean three currents were observed lying on top of each other, alternately flowing in opposite directions. Drifting stations and island observatories were also established for oceanographic studies of a comprehensive character. Many interesting observations of ocean waves were made that are of value for the understanding of the factors that produce not only normal waves but anomalous effects of different kinds such as hurricane waves, tsunamis (tidal waves resulting from submarine disturbances), and sea surges.

As with the Antarctic programme, it was clear that the co-operative effort in oceanography achieved during the IGY should be maintained, through the Special Committee for Oceanographic Research, SCOR, which is in full operation. Included among its major activities is an intensive international study of the Indian Ocean to be carried out during 1964–65. This ocean is one that has not hitherto been studied to any extent.

Conclusion

So many scientific activities were carried out during the IGY that it has not been possible to do more than indicate some of the most striking. An enormous number of data was accumulated covering a very wide range of subjects, and it is continuously yielding new information as analysis proceeds. Beyond this, the scale and success of the cooperation between nations in a peaceful enterprise is of lasting importance not only for the dramatic expansion in geophysics but for the example it sets for future cooperation in other spheres.

Acknowledgments

I am indebted to the Royal Society, and particularly to its Executive Secretary, Dr D. C. Martin, for much assistance in the provision of material. It is also a pleasure to acknowledge the use made of the valuable *IGY Bulletin* published by the National Academy of Sciences of the U.S.A., which provides a monthly survey of programmes and findings of the IGY and the IGC-1959 as related primarily, but not exclusively, to United States programmes.

Aflatoxin, the active principle in Turkey 'X' disease

P. C. Spensley

Mould infection of oil-seed cake has long been suspected as a possible cause of ill-health among farm animals, but only within the last three years has the problem been closely investigated. It has been found that groundnuts may become infected with strains of the mould *Aspergillus flavus* that produce a group of highly toxic substances known collectively as aflatoxin. This has in the past caused the deaths of large numbers of farm animals, especially young animals. There is, however, no evidence that human beings have suffered, and with recognition of the nature of the hazard, steps can be taken to ensure that there need be no danger from the substances in the future.

Well before the beginning of this century, the literature on the feeding of farm animals contained warnings that, though valuable as animal feed supplements, oil-seed cakes from the tropics were liable to be attacked by moulds and could thereby be rendered both distasteful and injurious. The cake produced by expressing the oil from groundnuts (peanuts, *Arachis hypogaea L.*) was one of those particularly referred to. Since then, groundnut cake has on a number of occasions been suspected as a cause of some outbreaks of livestock poisoning, but as such incidents were generally isolated and short-lived they were never thoroughly investigated. The possible association of mould infection with toxicity was forgotten. Three years ago, however, there occurred an outbreak of disease among poultry in Britain so serious that a thorough investigation was put in hand, which has since led to discoveries of great interest.

In 1960, poultry farms in the United Kingdom suffered severe losses of young turkeys and ducks, some 100 000 young turkeys dying in the course of a few months. The cause of the outbreak was not at first recognized, and as it was thought to be a new disease, this was tentatively named Turkey 'X' disease [1]. Affected birds died within a week, during which they lost their appetite, became markedly lethargic, and developed a weakness of the wings. A characteristic attitude of head, neck, and legs was adopted at the time of death. Post-mortem examination showed haemorrhages or pale necrotic lesions in the liver and, frequently, engorged kidneys.

As no evidence could be found that Turkey 'X' disease was infectious, the possibility of poisoning was considered. The feed of affected birds was examined thoroughly for bacterial toxins, inorganic poisons, possible organic contaminants such as insecticides and glycosides, and for plants or plant parts of a poisonous nature, such as castor bean. None of these could, however, be detected. It was then realized that a common factor in the outbreaks was the presence in the feed of material from a consignment of groundnut meal from Brazil—the first to have been imported into the United Kingdom from that country—and feeding experiments readily confirmed that this was indeed the cause. Samples of this consignment of groundnut meal were re-examined for contaminants of the kind referred to above, but none was found; it remained therefore to study the actual meal.

While this work was in hand, evidence was accumulating about the effects of this groundnut meal on other farm animals [2, 3]. Pigs and calves were both found to be susceptible, the symptoms and liver changes produced being very similar to those due to ragwort (*Senecio* spp.) poisoning. Ducklings proved to be particularly sensitive [4]. Within a few days of eating food containing toxic meal, destruction of the ducklings' liver parenchymal cells occurred, together with extensive proliferation of bile-duct epithelial cells. On the basis of these characteristic changes and of the rate at which they took place, a biological assay test for the groundnut toxin was devised [5], and this proved of great value in the work of extracting and concentrating the active principle.

By more or less conventional methods for concentrating unknown natural products, a ten-thousandfold concentration of the activity was achieved. It was then observed that the intensity of a characteristic blue fluorescence exhibited by the concentrates in ultraviolet light ran roughly parallel to the toxicity as shown by the duckling test. This led to the development of a chemical method for determining the presence and approximate concentration of the toxic factor [6], and by using this, the extraction work was further speeded. With the help of this method many more samples could be tested, and it was practicable to make a start on the examination of groundnuts and groundnut products from various parts of the world.

From these tests it soon became apparent that the toxic factor, far from being confined to certain batches of material from Brazil, was present in some of the samples obtained from each of the other producing countries. Additional support for this was simultaneously being afforded by the fact that further outbreaks of Turkey 'X' disease were being diagnosed, and were being shown to be caused by batches of groundnut meal from countries other than Brazil.

This widespread distribution of the toxic factor, coupled with the fact that only a proportion of samples exhibited toxicity, suggested that contamination by a micro-organism might be the cause. Investigation of this hypothesis soon revealed that strains of a commonly occurring mould, *Aspergillus flavus*, were responsible for producing the toxin [6]. Here, then, was a rediscovery of the fact that mouldy oil cakes could be injurious to animals; but this time scientific interest had been aroused and it was possible to take the matter much further.

From this point, work on aflatoxin, as the toxic factor had been named, branched out in a number of directions—microbiological, chemical, analytical, agricultural, toxicological, and commercial. Present knowledge of the subject can conveniently be summarized under these headings.

Microbiology of aflatoxin

Since the original isolation of a toxin-producing strain of *Aspergillus flavus* from a toxic sample of groundnuts, other strains of the species have been selected and studied. By far the greater proportion of these have not exhibited any ability to

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produce aflatoxin, but several—a dozen or more—toxin-producers have been identified, and are lodged for reference with the Commonwealth Mycological Institute. The mould does not produce a single toxin, but rather a mixture of closely related toxins, and the toxin-producing potential of these strains varies as regards both total production and the proportion in which the active components are synthesized.

Much work has been done on the artificial culture of the aflatoxin-producing strains. Initially, this was done on sterilized non-toxic groundnut kernels, a method that is still used. Later, synthetic media were studied, and some—particularly Czapek-Dox medium with added yeast extracts, and Raulins' medium—were found to give good yield of toxin. Addition of traces of zinc to the former medium increased toxin yield, particularly of one of the aflatoxin components. These methods have been used for the larger-scale production of aflatoxin for chemical and toxicological research.

A. flavus is a common mould; it can be isolated, for instance, from many stored dried foodstuffs and from tropical soils. It grows rapidly, but requires somewhat more moisture than most other moulds. At tropical temperatures (30°C), it will grow at 80–85 per cent relative humidity and above; this corresponds with moisture contents in groundnut kernels and defatted meals of about 9 per cent and 16 per cent or more respectively [16]. This knowledge is of great practical importance in considering control measures.

Also of considerable practical significance in devising means of control was the discovery that in any 'naturally' toxic batch of groundnuts, mould development and the toxic factor occur in a small proportion of kernels only, these generally being distinguished by having discoloured flesh. This will be referred to again later.

Chemistry of aflatoxin

For several reasons the part of the programme devoted to purifying the toxic factor and determining its chemical structure has run into formidable difficulties. Firstly, the aflatoxin content is only a few parts per million in even the most toxic samples of groundnuts, and concentration of the active material is laborious. This particular difficulty has been much reduced, however, by the artificial culture of the aflatoxin-producing organism on sterile groundnuts and synthetic media.

Secondly, the prolonged efforts to purify and characterize the toxic factor have shown that aflatoxin is, in fact, a complex of compounds apparently very closely related structurally [7, 8]. It is not yet certain just how many components there are; four seem quite well established, and two of these (now tentatively named aflatoxin B1 and aflatoxin G1) have been isolated in sufficient quantity for various physical and chemical examinations to be put in hand. Formulae of $C_{17}H_{12}O_6$ and $C_{17}H_{12}O_7$ have been suggested for these two components, on the basis of microanalysis and mass-spectrometric determination of molecular weight. Lactone and methoxyl groupings appear to be present, but free hydroxyls are absent. Other features of the structure are proving hard to elucidate, but it is hoped that current X-ray studies will be informative. Aflatoxin B1, which in chromatography is the faster-running blue fluorescent component, is highly toxic. The LD_{50}—that is, the dose required to kill 50 per cent of treated animals—is less than 20 µg for day-old Khaki-Campbell ducklings; this compound may be responsible for most of the toxicity in naturally toxic groundnuts. Aflatoxin G1—a compound with a greenish-blue fluorescence—seems to be less toxic, the LD_{50} for day-old ducklings being about 60 µg.

Another research communication [9] claims the resolution of extracts from toxic strains of *A. flavus* into at least twelve fluorescent components, five of which have been shown to be toxic to ducklings. In all this extraction and purification work the possibility of artifact production has to be borne in mind, particularly as it is known that at least one of the aflatoxin components is photosensitive and gives rise to other fluorescent substances. Alkali also produces changes which may, or may not, be reversible, according to the conditions of treatment. As will be seen later, this is significant in connection with the normal process of purification of groundnut oil.

Tests for aflatoxin

In all work of this kind, the development of a simple and satisfactory assay method, enabling the substance in question to be traced through a series of operations, is of the first importance. Mention has already been made of a biological test for aflatoxin using ducklings. In this method, the sample of groundnuts or groundnut products under test is defatted and then extracted with methanol. The solvent is removed from this extract, and the residue, after futher purifying by partition between immiscible solvents, is suspended in water and administered by polythene tube directly into the gizzard of day-old Khaki-Campbell ducklings. An amount of extract equivalent to 10 grams of the original sample of meal is given on the first day, and this dose is gradually increased so that, over a period of four days, the equivalent of 80 grams in all is given.

If the sample proves lethal within seven days of the start of the test, it is considered to be 'strongly' toxic. If the ducklings survive to the seventh day but show the liver lesions, the samples will be graded as 'moderately' or 'slightly' toxic according to the severity of the lesions. Aflatoxin concentrations down to 0·1 parts per million can be estimated in this way.

The discovery of a chemical test, based on the ultra-violet fluorescence of chromatographically purified material, has already been referred to. This has undergone many improvements since the original procedure was worked out. In the latest version of this test [10], the sample is defatted and then extracted with methanol. The extract, after removal of much of the solvent, is partitioned between water and chloroform; the chloroform layer is concentrated, and aliquot quantities chromatographed on thin layers of aluminium oxide. A blue fluorescent spot at R_f 0·5–0·6 is a positive indication of aflatoxin. A semi-quantitative estimation of its concentration in the original sample can be obtained either by comparing the intensity of the fluorescence with that from a known sample, or by spotting on to the chromatoplate a series of very small volumes and observing the point at which the fluorescent spot is only just visible to the naked eye.

The biological and chemical tests have generally been in good agreement with one another, and the later versions of the chemical test, with their better separation of components, are even more reliable. However, the possibility of a non-toxic substance having similar fluorescent and chromatographic properties must not be overlooked. For this reason, laboratories undertaking chemical tests for aflatoxin are advised to check, if possible, a small proportion of their 'positives' by biological assay. There appears, however, to be no doubt that if the chemical test is negative the sample is aflatoxin-free, at least down to the level of sensitivity of the test; if required, this could readily be as high as a few parts per thousand million.

Some encouraging results have been obtained in attempting to develop a simpler biological test using hen's eggs, and this might eventually serve as the check test referred to in the previous paragraph. In this method [11], batches of fertile hen's eggs are incubated for five days and portions of the extract under test are then injected into the yolk sacs. If, after

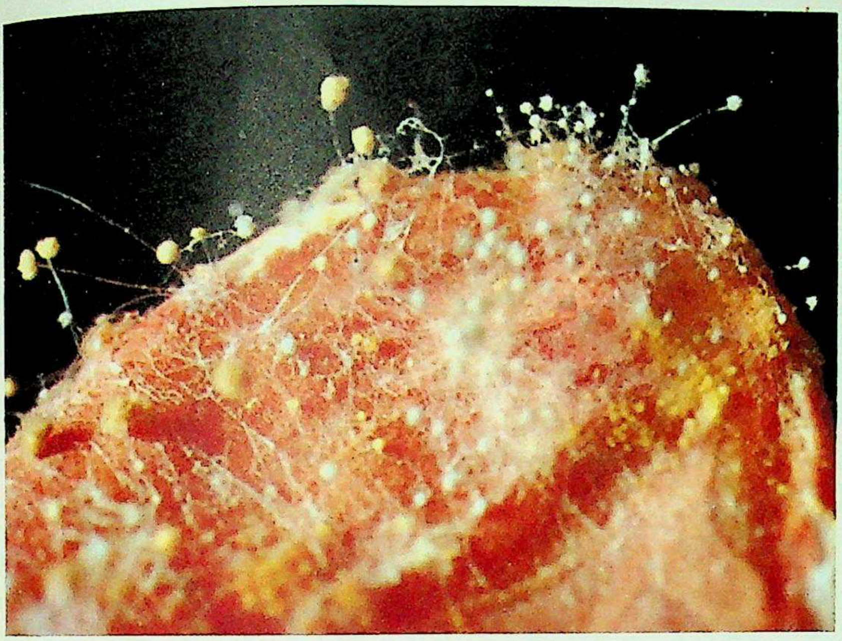

Figure 1 *Photomicrograph of an infected groundnut. (× 25)*

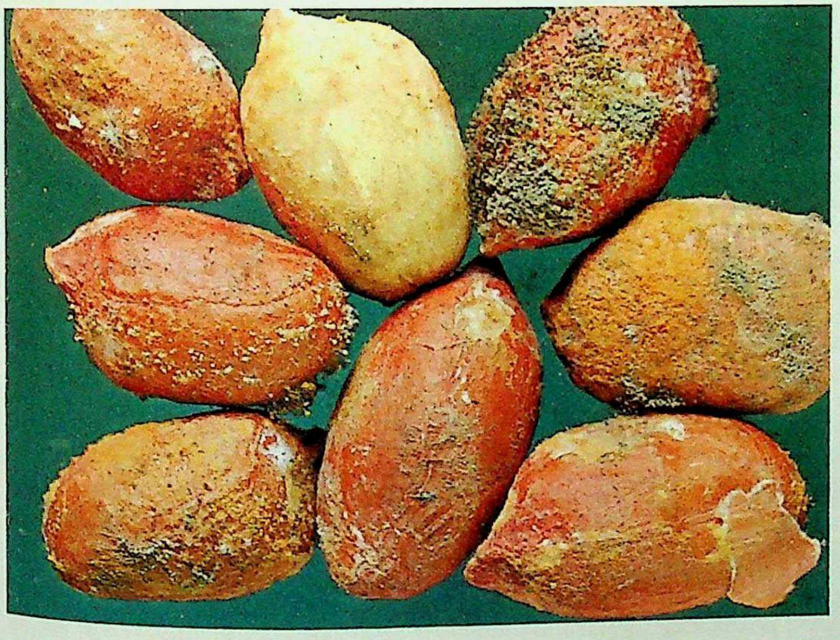

Figure 2 *Infected groundnuts. (× 2·5)*

a further two days' incubation, the embryos are dead, the sample is considered toxic. Chick embryos are highly sensitive to aflatoxin, fractions of a microgram being fatal. The possibility of using this as a semi-quantitative assay method is being investigated.

Agricultural aspects

As soon as it had been established that the toxicity of certain batches of groundnuts was due to mould attack, it became important to discover the point, or points, at which the mould spores gained access to the groundnut kernels and at which they developed and produced the toxin. Investigations were at once started in several African countries.

It was already clear that since *A. flavus* will grow only when sufficient moisture is available, aflatoxin production can in the first instance take place on groundnut kernels only before the post-harvest drying brings the moisture content below the critical level mentioned earlier. Mould growth might, of course, take place also at any later stage if the moisture content of kernels, cake, or meal rose above the critical level. Subsequent drying would not affect the aflatoxin content, as the substance is stable under normal drying conditions.

While the nuts are still in the ground, their moisture content is high (at least 25 per cent), but, despite this, mould development seems normally not to occur at this stage. Apparently the healthy growing nut has a protective mechanism against mould growth, and this may be supplemented by the physical barriers to spore penetration afforded by the intact shell and the seed coat. If, however, the nuts are left unharvested beyond maturity, mould attack can occur in the ground and may be serious. Insect attack on the nuts may contribute to the trouble by breaking down the natural barriers.

Probably the most critical stage is that immediately following harvest. The nuts are still of high moisture content when lifted, and unless both atmospheric conditions and harvesting practice are good, drying to the safe moisture level may not take place quickly enough to avoid significant mould development. In some countries and regions, harvest may take place when rains are still about; in others, farmers may not take sufficient care to secure rapid and complete drying, and they may fail to use recognized techniques of stacking plants in the field after harvesting. In either circumstance, and particularly where there is a combination of both, the risk of mould infection, and consequent aflatoxin development, is severe.

Relevant in this context is the observation, already referred to, that even in toxic batches of groundnuts, the toxicity normally affects only a minor proportion of the kernels. One or more factors that tend to affect only a small proportion of nuts must therefore be important, as well as the general conditions indicated above. One such factor appears to be the damage to the shell that some nuts inevitably sustain at, or soon after, harvest. There is experimental evidence that the kernels from broken shells are more toxic than those from intact shells. Such damage may both facilitate entry of mould spores and provide a more favourable environment for their subsequent growth.

From the above it is obvious that the practice employed in a few areas of shelling the nuts before drying is very hazardous, unless rapid drying is possible. Again, the practice employed in some regions of deliberately wetting nuts before shelling and during crushing may also be hazardous.

If groundnuts are harvested and dried satisfactorily, there will be no further opportunity for mould growth on the kernels or on cake or meal prepared from them, unless they are exposed to conditions that permit the moisture content to rise again above the critical levels. In areas where the atmospheric relative humidity is above 85 per cent at certain periods of the year, dry storage is necessary if mould infection is to be prevented. Even in somewhat drier areas, protection from local wetting by rain or condensation is necessary. Similar requirements apply during transport.

There is a little evidence that crops other than groundnuts —maize, for instance—may, under adverse conditions, be attacked by *A. flavus* and so be rendered potentially toxic. However, such infections probably represent only a very small minority of foods and animal feeding stuffs that become infected with mould. Nevertheless, there is undoubtedly scope for further investigation.

Toxicology of aflatoxin

It has already been mentioned that cattle and pigs are susceptible to toxic groundnut meal, as well as turkeys and ducks. Feeding trials, however, revealed that sensitivity to aflatoxin varies considerably from one species to another, although, in all cases, the young animal is much more susceptible than the corresponding adult. Among poultry, ducklings are highly sensitive, young turkeys somewhat less so, and chickens comparatively resistant. Of the farm mammals, piglets appear to be the most sensitive; young calves also are highly susceptible, but lambs much less so. In all species, the principal site of toxic action is the liver.

In order to devise appropriate control measures, it is important to know with fair accuracy the dietary levels of aflatoxin below which no adverse effects will be produced in farm animals of various species and ages. The extensive long-term feeding experiments necessary for this are now in hand. The whole picture is somewhat complicated, however, by the fact, already stated, that aflatoxin is a mixture of several components of varying toxicity, and that these may not always be present in the same proportion.

A number of toxicological studies on 'naturally' toxic groundnut meals, and on isolated aflatoxin, have already been conducted using common laboratory animals. Now that ways have been found for separating and purifying the individual components, much further work will be necessary to establish the importance of each of these. The possibility of synergism between components will also have to be examined.

In the course of these laboratory studies, rats have not shown the acute toxicity signs seen in ducklings and young turkeys, but when fed small amounts of toxic groundnut meal for periods of six months, they have developed primary carcinoma of the liver [12]. It has yet to be established that this was due to the aflatoxin complex, though this seems virtually certain. It is also important to learn whether this is just a reaction peculiar to the rat, or whether it may occur in other species.

Naturally, the possible consequences to man have to be carefully examined. To get the best possible idea of what man's reactions would be if exposed to aflatoxin, a study of both acute and chronic effects in monkeys is necessary. Some preliminary work on this is in progress in Britain, and a more extensive investigation is shortly to be started in India. These will undoubtedly provide most valuable information, though the feeding of sub-acute doses of toxin to monkeys may have to continue for a number of years before the trial can be considered complete.

It should be emphasized that there is as yet no evidence to suggest that man has suffered ill-effects from aflatoxin through consumption of groundnuts and groundnut products. Had this occurred in Britain, for instance, and assuming that the human reactions to the toxin would be similar to those observed in animals and birds, some evidence of increased incidence of the corresponding morbid conditions might have been detectable over the years. No such evidence is afforded by the vital statistics, but it must be remembered that there is no reason to suppose that Britons are ingesting, or have ingested, significant quantities of aflatoxin.

It is interesting to note that prior to the recognition of Turkey 'X' disease and the isolation of aflatoxin, *Aspergillus flavus* had been implicated in a few cases of animal poisoning, and in these, the mould had developed in other materials than groundnuts. For example, J. E. Burnside and his co-workers [13] isolated a strain of *A. flavus* from mouldy corn that was suspected of killing hogs, and they grew it in pure culture on autoclaved corn. The product proved toxic to swine and mice. Y. I. Kulik [14] found mouldy peas to have been infected by *A. flavus*, and a fraction prepared from this killed cats and rabbits.

It is also noteworthy that the exudative hepatitis observed in guinea-pigs that had been fed the Bruce-Parkes Diet 18, described by Paget, has now been shown [15] to be due to the groundnut meal ingredient of the diet having been contaminated with aflatoxin.

Commercial and other aspects

Foods based on groundnuts are attractive as protein-rich ingredients for animal feeding: the protein content is high, the protein is of good nutritive value, and the price is favourable. Imports to the United Kingdom in 1961 approached 600 000 tons (value £18 million), somewhat more than half coming from India. In addition, 90 000 tons were produced from groundnuts crushed in Britain. These commodities are, therefore, an important item of trade.

After the Turkey 'X' disease outbreak in 1960, the animal feeding stuffs industry in Britain quickly adjusted itself to the knowledge as it was gained. A voluntary code of practice for dealing with groundnut cake and meal was recommended by the trade association mainly concerned. This advised, firstly, that all consignments should be tested for aflatoxin, and, secondly, that no more than certain percentages of the material should be included in rations for various types of stock, according to the aflatoxin levels found. These percentages were based on the information about farm-animal susceptibility then available, and will doubtless be revised in the light of further knowledge. Meanwhile the desired effect seems to have been achieved, as the number of reported outbreaks of 'X' disease among poultry and the larger farm animals has been greatly reduced.

Regarding the groundnut products of commerce designed for human consumption, the picture is reassuring. Refined groundnut oil, which is used extensively for margarine manufacture and cooking purposes, is always toxin-free, even if it has been produced from contaminated nuts. This is because any trace of aflatoxin that may have found its way into the crude oil is removed by the alkali wash employed in the refining process.

Edible peanuts in Britain are always of the 'H.P.S.' (hand picked selected) grade, and no sample of such material has yet been found to be toxic. This arises from the fact, referred to already, that in toxic batches of nuts the toxin resides in a small proportion of the nuts only, and that these are almost always damaged, discoloured, or obviously mouldy. Such inferior nuts are removed in the hand picking process. Peanut butter is always manufactured from H.P.S. grade nuts, and so is equally toxin-free.

Finally, we should mention the use of groundnut protein for human supplementary feeding, particularly for infants and young children. This is usually in the form of groundnut flour, containing about 50 per cent protein. Groundnut protein—especially when mixed with a minor proportion of another protein, such as casein—is of high nutritive value and, being also one of the most readily available sources of concentrated vegetable protein, could undoubtedly help very considerably with the malnutrition problems in certain regions.

In India, where a 'multi-purpose food' based on groundnut flour is now being produced, an uncontaminated product is being secured by a thorough hand selection of nuts before preparation of the flour; testing for aflatoxin has recently been introduced as a further safeguard. It is to be hoped that many other units of this kind will be introduced into groundnut producing areas, and that much more of this very valuable material will be made available for human feeding in various parts of the world.

Conclusion

It will be clear from what has been said above that many questions regarding aflatoxin remain to be answered. How many natural components are there, and what are their chemical structures; why and by what biochemical processes is aflatoxin produced by certain *A. flavus* strains; can simpler chemical and biological test procedures be devised; what is the mode of action of aflatoxin in animals?

The most important, practical question is, however, what can be done to prevent aflatoxin being present in groundnuts and groundnut products for animal and human feeding. There seems little hope of finding an economical way of deactivating already toxic groundnut cake or meal, and though hand picking may be effective where whole nuts are concerned, this too is costly; possibly the process could be mechanized. The most urgent need, therefore, is so to improve agricultural, storage, and transport practices in producing countries that mould contamination is negligible in the first place. This is an enormous undertaking, but one that happily is already receiving attention in some countries.

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NO Dr. S. Dutt ?

The function of the hippocampus

John D. Green

Although our knowledge of the physiology of the sense of smell is imperfect, compared with that of the senses of sight and hearing, recent work has added much to it. It is now clear that the parts of the brain that were originally concerned only with the sense of smell have acquired many other important functions concerned, for example, with the appetite for food, with the activity of the ductless glands, and with regulation of blood pressure. This extension of function has presumably occurred as a result of the importance of the sense of smell to the primitive hunting animal.

In most animals the sense of smell has remained one of the most dominant of all the special senses, and even in man it is of exceptional importance. Although the human sense of smell cannot be compared in acuity with that of the dog, the human ability to associate ideas with odours is much more complicated. Odours can affect us emotionally, as when the odour of a school classroom or hospital corridor suddenly recalls some former experience vividly. They may influence us in more subtle ways, which may not directly affect our conscious minds. The sense of smell is not constant in an individual. J. Le Magnen [1] has shown, for example, that women can detect the presence of 17-keto steroid compounds in urine, but this ability is apparently dependent on the integrity of the subject's own ovaries, for it is lost after ovariectomy and restored by administration of female sex hormones. The ability is, in fact, closely related to the reproductive state. One may speculate that, while the transducer that translated the presence of chemicals into nervous impulses may have been very sensitive in lower animals, the resulting patterns of activity it could produce became progressively more elaborate as more complex brains evolved.

Comparative studies of the olfactory organ itself, such as those of A. C. Allison [2] and W. E. Le Gros Clark [3], suggest that this transducer has not undergone the same degree of specialization as, for example, the eye. The olfactory epithelium is surprisingly and deceptively simple in appearance. The number of primary olfactory receptor cells is very large—over 100 million in man—but their appearance differs very little from one vertebrate species to another. These receptor cells are provided with small tufted sensory appendages on the exposed surface of the olfactory epithelium; a surface view of these structures, seen under the microscope, is like a child's drawing of a field of daisies. The receptor cells are bathed by the secretions of small glands and are embedded in a matrix of supporting cells. Each receptor sends a fine process to the brain, where, in the olfactory bulb, it establishes contact with a second-order neuron (figure 1). The information transferred from one nerve cell to the next is believed to be carried by means of a specific chemical substance. The junction of two neurons is called a synapse; in most cases, these synapses are between the transmitting fibre (the axon) of the cell sending information and the receiving processes (dendrites) or the main body (soma) of the receiving cell. Sometimes several cells send processes to one receiving cell, but the degree of this convergence is usually limited to a few connections.

The first olfactory synapse is unique. Each synapse is a remarkable tangle of incoming axons and receptive dendrites. The synapses, known as glomeruli, are so large that they are visible to the naked eye. They are, indeed, so large that there are small nerve cells connecting one part of a synapse to another and one glomerulus to adjacent glomeruli. Strangely enough, it was largely on the basis of these exceedingly complicated olfactory glomeruli that Cajal was able to establish the neuron doctrine. To each glomerulus pass about 25 000 axons from the receptor cells (figure 1). This vast influx is passed on to fewer than 100 second-order cells, and of these only about 25 continue to the brain; the rest pass over to the opposite olfactory bulb. The convergence of information is, therefore, almost in the ratio of 1000 : 1; the message of 100 000 000 receptors reaches the brain through a mere 100 000 axons of the so-called mitral cells. The axons of the mitral cells pass to the part of the cerebral cortex called the pre-piriform cortex, but what happens next is by no means clear.

In teaching physiology to medical students it has long been customary to postulate a complex series of pathways representing the course of the olfactory impulses (figure 2). As there is now experimental evidence that such pathways really exist, there seems to be no particular reason to give up the old name of rhinencephalon (literally 'nose-brain') for the part of the fore-brain traditionally associated with the sense of smell. Nevertheless, many other connections are involved, and the paths have been traced so far from the primary neurons that there is reason to doubt that the rhinencephalon is entirely, or even mainly, concerned with the detection of odours. The tendency of these 'olfactory' paths to form wide loops, sometimes apparently feeding back to the point of origin, is well seen in these pictures.

A brief digression into comparative anatomy helps to unravel some of these complexities. The whales and their close relatives, the dolphins and porpoises, have lost their olfactory senses. Nevertheless, they have retained important parts of the rhinencephalon and, notably, the hippocampus, which seems to represent the cortex in its most primitive condition. Indeed, the rhinencephalon to some extent seems to represent the primitive cerebral hemisphere.

Animals such as fish and amphibians whose cerebral hemispheres consist chiefly of rhinencephalic structures are able to respond to stimuli in a bewildering variety of ways; we must suppose that the rhinencephalon, which we can equate with the primitive hemisphere, early assumed functions far different from the detection of smells of various kinds. As far as is known, destruction of the olfactory nerves, olfactory bulbs, or the olfactory tracts between the bulbs and pre-piriform cortex results only in the loss of the ability to smell, but destruction of the pre-piriform cortex or structures further along the rhinencephalic path has more serious effects.

John D. Green, *M.A., D.M.*

Was born at Guildford in 1917 and was educated at City of Oxford School and St John's College, Oxford. After three years in Cambridge at the Anatomy Department, he went to the United States on a Blaine Fellowship and has worked there since that time at Wayne University and the University of California, Los Angeles, where he is now a professor of anatomy. He has worked on the comparative anatomy and physiology of the nervous control of the pituitary gland and various neurophysiological problems connected with the rhinencephalon.

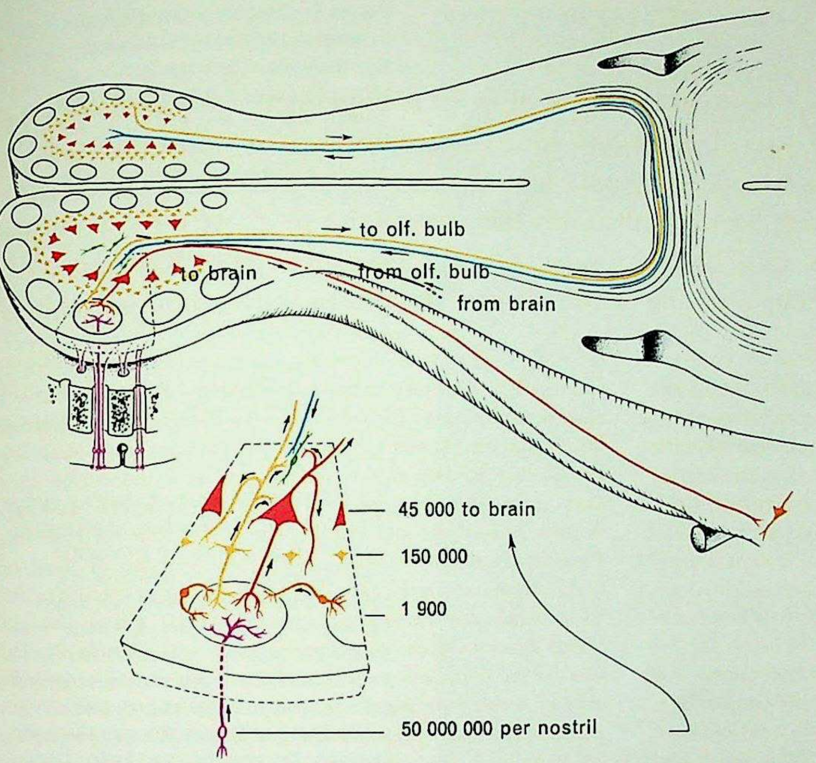
to olf. bulb
to brain
from olf. bulb
from brain
45 000 to brain
150 000
1 900
50 000 000 per nostril

Figure 1 *Diagram showing some of the principal connections of the rabbit olfactory bulb. The purple olfactory receptors synapse at the white circles (the glomeruli) with two principal kinds of cell, the mitral cells (red) which connect with the brain, and the tufted cells (yellow) which connect with the opposite bulb. In addition, short interconnections occur in the same bulb (orange cells in insert) and fibres come from the opposite tufted cells (blue) and from the brain (white) to moderate the activity of the bulb. The cells exert a marked influence on each other before the brain receives the results of the olfactory stimulus.*

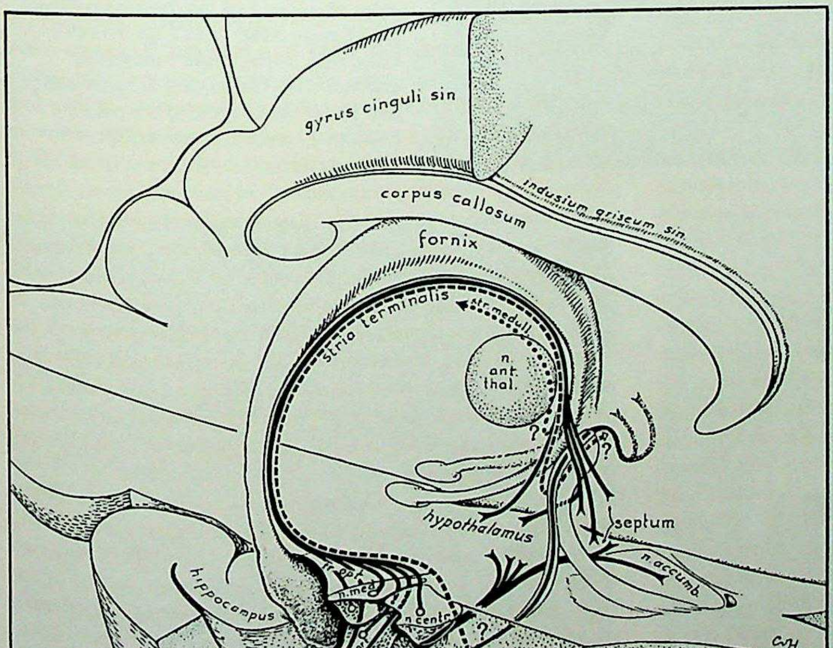
gyrus cinguli sin
corpus callosum
indusium griseum sin
fornix
stria terminalis
str. medull
n. ant. thal.
hypothalamus
septum
n. accumb.
hippocampus
tr. opt.
n. med.
n. centr.
n. cort.
n. bas.
n. lat.
lobus
lobus temp
pirif.
tr. olf. lat.
n. str. olf. lat
GvH
olf. bulb (mid-line surface)

Figure 2 *This figure shows some of the principal connections of the rhinencephalon. It does not represent the brain of the rabbit, but the approximate location of the same structures in the rabbit brain is shown in the insert, and the connections are much alike. Note the lateral olfactory tract entering at the right (the anterior end). The tendency to form closed loops of connections is clearly seen [13].*

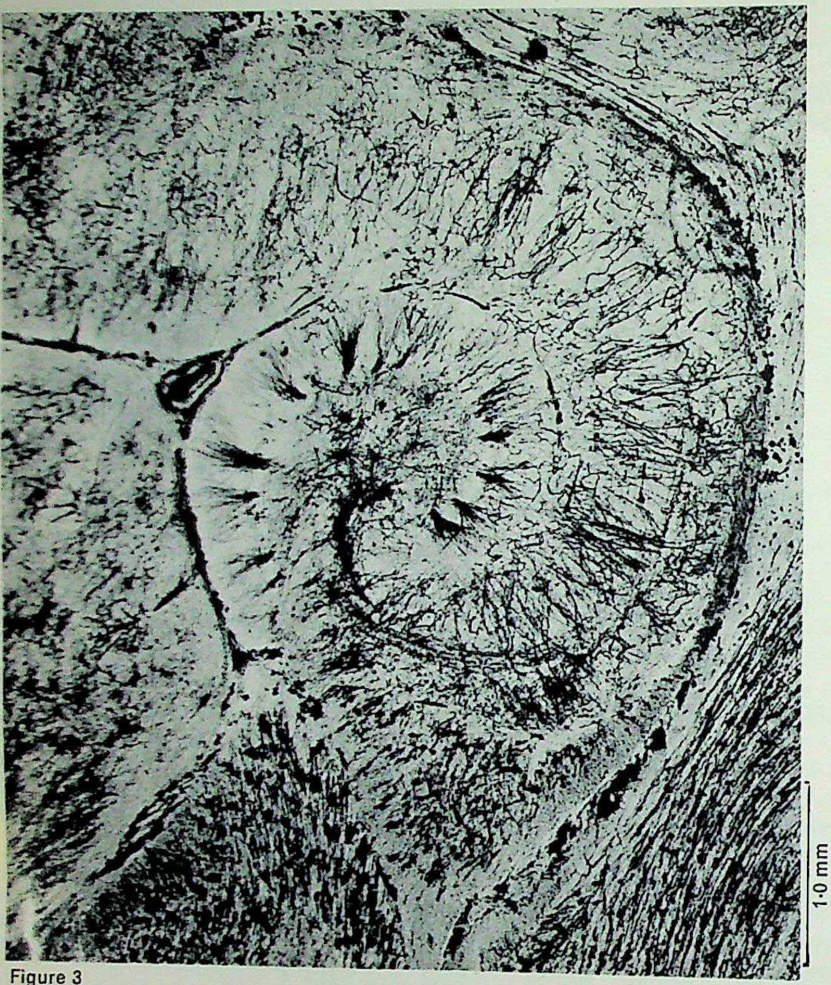

Figure 3

Figure 3 *Snail-shaped outline of a transverse section of the monkey hippocampus. The more detailed view shown in figure 4 would correspond roughly with an area just above and to the right of the most central large circular structure (the gyrus dentatus). (Diameter about 5 mm.)*

Figures 4 and 5 *Figure 4 shows a section through a part of the rabbit hippocampus, in which the neurons are arranged in rows like soldiers. The bodies of the soldiers are the apical dendrites, which have many branched feet; the heads are the cell bodies. From the heads spring tufts of basal dendrites studded with small dot-like structures called gemmules. The axons of the cells pass through this layer vertically, but are obscured by the basal dendrites.*

Figure 5 shows, for comparison, a section through about half the thickness of the rabbit neo-cortex. Notice the variety of cells, with innumerable overlapping connections. The surface is to the right, and the axons of most of the cells are directed to the left, towards the centre of the brain.

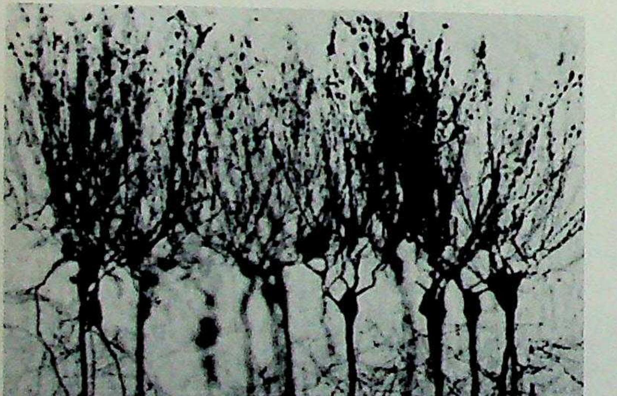

Figure 4

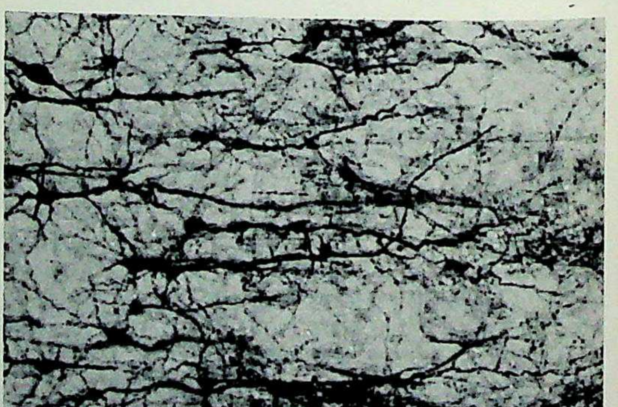

Figure 5

The temporal lobe

The rhinencephalic path enters a part of the brain called the temporal lobe—a large section of the cerebral hemisphere lying in the general region of the temple—at the point where the lateral olfactory tract enters the pre-piriform cortex. The temporal lobe is divided by a fissure (rhinal fissure) into two regions: one is of ancient origin, and the other, forming the greater part in man, is the neo-cortex. In man, at least half the cerebral cortex may be removed surgically, or destroyed by disease, with surprisingly little effect. Removal of parts of the temporal lobes, however, leads to dramatic personality changes. This is particularly so if the removals include both sides and also rhinencephalic structures. As early as 1888, S. Brown and E. A. Schaeffer [4] described many of these effects in experimental animals, but little attention was paid to their work. About 25 years ago, the importance of the temporal lobe was rediscovered by H. Klüver and P. C. Bucy [5] and by P. Bard and V. B. Mountcastle [6]. In recent years, the importance of specific parts of the temporal lobe has begun to be recognized, particularly of the rhinencephalic structures, and structures such as the amygdala, that are connected with the rhinencephalic areas. These 'ancient' parts are now known to influence bodily activities not under conscious control, as well as behaviour. Specifically, there is evidence that they are concerned in appetite for food, control of the activity of the ductless glands, and regulation of blood pressure.

Behavioural effects due to removal of the temporal lobes were described in some detail by Klüver [7], who found that monkeys become unusually tame and showed a strong tendency to investigate unfamiliar objects, especially by putting them in their mouths. A loss of fear seemed to be another peculiarity. Monkeys, in general, are frightened by snakes, whether real or artificial. Klüver demonstrated that after temporal lobectomy, monkeys previously terrified by snakes would grasp a snake presented to them and lick it or put its head into their mouths. The animals appeared to be quite alert, but were constantly investigating objects in this rather bizarre way; they repeatedly put inedible objects in their mouth, only to reject them and try once more. Changes in dietary habits and changes in sexual behaviour were also notable. Although the results of Bard and Mountcastle were not precisely like those of Klüver and Bucy, they also produced dramatic changes; they emphasized particularly that angry or aggressive behaviour occurred in cats after removal of temporal lobes. Many investigators consider that the differences in the observations of the two groups are due to species differences or to minor differences in operative technique.

Interest was again aroused by L. Schreiner and A. Kling [8]. They removed the amygdala, and with it the overlying cortex, in several species and saw as a result hypersexualism; hyperphagia (excessive eating); changes from vegetarian to carnivorous or omnivorous diet in the monkey; and, like Klüver and Bucy, a general taming of the experimental animal. Schreiner and Kling thus were able to produce much the same results as Klüver and Bucy, but after removing very much less brain tissue from the same region.

Our first work on this problem was to see if by reducing the injured area still further we could obtain the same effects or perhaps induce only one effect at a time.

We found that we could obtain abnormal sexual behaviour in cats as a result of brain lesions less than one millimeter in diameter, and restricted to the piriform area in a region in which the olfactory nerves can be expected to terminate. These sexual abnormalities were not accompanied by other obvious changes unless the damage encroached upon the amygdala. In that case, several other effects were produced: hyperphagia, which seemed to be a primary effect; epileptiform fits (associated with behaviour changes of various kinds); and catatonic changes in which the animal assumed a rigid posture even when handled. These last two effects were thought to be due to secondary damage to other areas of the brain resulting from incidental damage to their blood supply, which passes through the injured region. The epileptiform fits were always associated with damage to the hippocampus, and the catatonic effects with damage to branches of the middle cerebral artery which pass through the front of the amygdala to supply the basal ganglia and internal capsule; the latter are parts of the brain concerned in voluntary movement. In these cases, flame-shaped areas of destruction due to loss of blood supply were always found in the internal capsule or basal ganglia, or both.

At first sight, the changes in reproductive behaviour seemed to represent a kind of *furor sexualis*, for the cats would try to mate not only with other cats of the same sex but with other species, including rats and guinea-pigs. However, with better knowledge of the normal mating habits of cats in captivity—and especially with recognition of the fact that the male cat will not mate until he has established a territory—we reached the conclusion that the change that had taken place was not so much a development of hypersexuality as a loss of discrimination or a loss of normal social behaviour in the cat. It did not seem to be related to the activity of the ductless glands that control the state of the reproductive organs.

Since the lesions we had made involved rhinencephalic structures, we became interested in the role the sense of smell plays in adaptation to a particular territory in a normal animal. A variety of experiments in which the male was either allowed to smell the female without seeing it, or conversely to see it without smelling it, indicated that in this context the sense of smell was of less importance to the male than was sight. As we cannot tell if the sense of smell was disturbed in the animals with lesions, we cannot say if it is important in the abnormal behaviour that the lesions produced. However, the influence of seeing was clearly important in the normal animal, and it may reasonably be asked whether or not there is a convergence of visual as well as olfactory data somewhere in the rhinencephalon. Probably there is, but the evidence for this convergence of information is clearer for the next section of the rhinencephalon to be considered, namely the hippocampus. Before we leave the piriform cortex, however, the possible significance for humans of findings of this kind may be mentioned.

One of the most common types of epilepsy is believed to originate in the temporal lobe of the brain, and removal of an epileptogenic focus sometimes benefits sufferers. The effects on cats of removal of restricted regions of the temporal lobe are, however, a warning against radical surgery in this part of the brain. It seems to be the consensus of opinion that while the effects of unilateral operation may not be very serious in humans, bilateral removals or lesions are much more dangerous. A case was reported by H. Terzian and G. Dalle Ore [9] in which all the characteristics of the Klüver-Bucy syndrome occurred in the patient as a result, and in Japan several similar cases have been described [10]. Since the removal of an epileptogenic focus is not infrequently followed by the appearance of a focus in the corresponding position on the opposite side, the surgeon may be tempted to operate again, especially if the results were good the first time. Probably it is not advisable to do so.

The hippocampus

Removal of the temporal lobe also involves removal of the hippocampus, or Ammon's horn. Unlike those in other parts of the brain, the cell bodies in the hippocampus tend to be closely packed, and their dendritic and axonal processes are found in exactly stratified layers. It is a most favourable part of the brain for studying the relation of different parts of the neuron to the flow of currents produced by the activity of different parts of the cell. The reason for this is that because the neuron processes overlap (figures 3–5), it is possible to obtain a kind of statistical sample of these currents in a way impossible in other parts of the brain. A peculiarity of the hippocampus is that it is the part of the brain in which what are called seizure-discharges are most easily induced. These are electrical events that can be recorded in the brains of epileptics or after prolonged electrical or drug stimulation of some parts of the brain of normal people. Finally, in many animals the hippocampus has an unusual kind of spontaneous electrical activity of a slow-wave nature. The cause of slow waves and seizure discharges is not precisely known, though they are of great diagnostic importance. Hippocampal slow-wave activity is less simple in animals with a highly developed neo-cortex than it is in other species. Possibly this may be because the neo-cortex is in some way capable of interacting with the hippocampus and so altering or complicating its activity. Whatever the reason, it is curious that, in animals like rabbits, the response of the hippocampus to strong electrical stimulation is quite different from that of the neo-cortex.

Hans Berger [11] originally showed that in man various stimuli, or even voluntary cerebration, would block the alpha rhythm of the neo-cortex. This means that the normal electroencephalogram recorded from the occipital region, for example, changes from a rhythmic high-amplitude sinusoidal activity at 9–12 c/s (the alpha wave) to a lower amplitude, faster (20–30 c/s), and more irregular activity (the beta wave). This desynchronization can be produced in experimental animals by a sound, a sight, an odour, or a touch. In the neo-cortex of subprimate animals the reaction to the same variety of non-specific stimuli is usually a little different from the alpha block of man. In such animals there occurs a somewhat similar interruption of intermittent trains of waves close to the alpha frequency. These trains of waves increase and then decrease in amplitude; because of their outline when recorded they are called 'spindles'. A non-specific stimulus of the kind described thus desynchronizes the neo-cortex in both man and lower animals. Since this desynchronization is associated with what appears to be a more alert state, it has been called the arousal reaction by G. Moruzzi and H. W. Magoun [12]. These authors postulated that the neo-cortex was controlled by a region of the brain-stem—which they regard as a functional rather than an anatomical entity—coinciding roughly with the reticular formation of anatomists; the term reticular activating system has been used for it. On this network of cells and fibres afferent impulses converge from all over the body. Instead of a neat parcelling of impulses of different kinds, as in the classical sensory paths, there seems in the reticular activating system to be a mixing of information. Destruction of this region usually leads to coma lasting for two or three weeks.

These important findings focused attention on the inadequacy of the older and oversimplified concepts which implied that the centres of consciousness and ratiocination were necessarily in the cerebral cortex. The considerable attention devoted to this subject in the last thirteen years has indicated that the present concept, too, is an oversimplification. Nevertheless, this, together with Berger's observation of the 'alpha block', lead to a new and much more objective method for assessing whether a subject is mentally alert or not. As yet, less attention has been focused on the behaviour of the more primitive 'olfactory' cortex. It, too, shows certain interesting correlations. In the rabbit, the slow-wave activity of the hippocampus is synchronized rather than desynchronized. It is possible to produce synchronization in the hippocampus of the rabbit by exactly the same stimuli as those which produce desynchronization in the neo-cortex. Although this effect is much harder to achieve in animals with better developed neo-cortices, such as cats and monkeys, the response occurs in many other species as well.

If electrodes are implanted into a rabbit's brain so that the activity of the hippocampus can be recorded in a conscious and virtually unrestrained animal, it is possible to test a variety of other stimuli. We observed that such a rabbit would at first respond to a gesture of the hand by producing a good train of waves, but that if this stimulus was repeated monotonously, at intervals of about 30 seconds, the length of the wave-train became shorter until it eventually disappeared. If the stimulus was then slightly varied—for example, by waving the hand back and forth instead of from side to side—the wave-train reappeared. Clearly, during this period of habituation, there were some changes in the brain. If the same experiment was repeated on successive days, the rate at which the animal adapted itself increased, suggesting familiarization; it was concluded that memory played a role in adaptation.

We also tried such naive experiments as observing whether or not the visual stimulus of seeing a cat would be much stronger than waving a hand: experiment showed that it was. Another simple experiment was to try the effect of different pitches of sound in producing desynchronization. Although it is well known that dogs can hear very high-pitched sounds, far beyond the human range, it was interesting to see that the rabbit stopped responding at about 6 kc/s, though the experimenter could hear the sound up to 14 kc/s. Much more sophisticated experiments are now being done from a psychological and conditioned-reflex standpoint, particularly by Grastyan in Hungary and by Adey in the United States.

To establish conditioned reflexes that depend on the detection of odours, we know that the olfactory receptors, the olfactory bulb and tracts, and the piriform cortex are essential, but not other parts of the rhinencephalon. It is not surprising to find that when this most intricate machine is stimulated or damaged some quite unexpected results are produced. We should not be astonished to find that within the rhinencephalon we can detect reactions to stimuli that are quite different from odours.

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The shapes of viruses

R. C. Valentine

The study of the detail of viruses by high-resolution electron microscopy was originally undertaken with the object of determining their shape. It led, however, to the detection of what appeared to be small sub-units of the protein coating. Their symmetry was studied, and this article describes the theories of the formation of viruses and of the nature of antigens that the study has suggested.

Ideas about the nature of viruses have changed over the years; even today there is still doubt as to whether a number of important points have been finally settled. The name shows that viruses were originally conceived of as poisons, for, unlike the living microorganisms that can also cause disease, they were invisible under the microscope and passed through filters as would a chemical. However, after the discovery that viruses multiply during the course of a disease, it became orthodox to view them as sub-microscopic forms of life. Some of the viruses were then crystallized, and the hypothesis that gained favour was that viruses form a link between living and non-living things; an example, it was even suggested, of the way in which life first emerged from an inorganic world. But the pendulum of speculation has recently swung back a little. The chemical nature of many simple viruses is now well established as a protein shell around a core of nucleic acid that is the essential genetic material. In some cases the nucleic acid extracted from a virus can itself start an infection. But no virus can grow, or indeed show any sign of life, until it is taken into a living cell—life could not therefore have started from anything like a virus. A simple virus is now seen as a macromolecular structure of nucleic acid and protein, capable of priming a suitable cell with genetic information. The infected cell then produces exact replicas of the virus.

Thus stated, the nature of viruses looks very different from that of a living microorganism. But some viruses are chemically more complex than simple nucleoprotein; and some bacteria can multiply only inside living cells. Indeed, the causal agents of a number of diseases still present problems of classification: are they to be called complex viruses, or are they bacteria that have carried their parasitic existence in cells to the extreme limit? Such problems raise questions as to how fundamental and absolute the distinction between viruses and bacteria is; for example, could a bacterium ever degenerate to a virus?

But whatever their origins, and quite apart from the diseases they cause—of special concern, since these cannot be checked with antibiotics—viruses have a fundamental interest as products formed in living cells in response to the presence of foreign nucleic acid. What is seen by examination of viruses with the electron microscope is therefore relevant to some basic biological problems.

Virus particles in profile

Work done some 20 years ago on the morphology of virus particles seen with the electron microscope was limited by the very poor contrast in the pictures. It was, however, found that of the viruses then available in suitable form, plant viruses could be either round or rod-shaped, while almost all animal viruses were apparently round. In 1957 K. M. Smith and R. C. Williams were working on a crystallizable insect virus (*Tipula* Iridescent Virus). To increase the contrast in the electron image they used the important technique of metal shadowing that had been introduced by R. C. Williams and R. W. G. Wyckoff in 1946. Metal shadowing gives an appearance in the electron microscope analogous to that of an object lit obliquely with a beam of light: with this technique Williams and Smith showed that the *Tipula* Iridescent Virus has a six-sided outline and throws pointed shadows [7]. About this same time I was trying to increase the contrast in micrography of the adenovirus, the virus that causes feverish respiratory infections in man. The technique combined phosphotungstic acid or uranyl acetate chemically with the virus. This treatment darkened the image of the virus particle sufficiently to show that it, too, has a six-sided profile (figure 2) [8]. These similar findings led to a study of the shapes and profiles of various geometrical solids and the shadows they throw to see which consistently appears to have a six-sided profile in all orientations.

The very regular hexagonal outline given in the electron microscope image by the *Tipula* Iridescent Virus and the adenovirus suggested that the virus particles have a shape nearly that of a perfectly regular solid, that is one with all its faces identical and its sides and angles equal. Euclid proved that there can be only five perfectly regular solids: these are the tetrahedron, the cube, the octahedron, the dodecahedron (whose twelve faces are pentagonal) and the icosahedron (whose twenty faces are equilateral triangles) (figure 1). Of these solids, only the icosahedron gives a hexagonal profile in most orientations. Williams and Smith elegantly demonstrated that the oblique shadows thrown by the icosahedron on to a flat surface on which it rests fitted exactly with the pictures of the metal-shadowed *Tipula* Virus [7]. Similarly the icosahedron was the only solid whose profile fitted well with the images of the adenovirus.

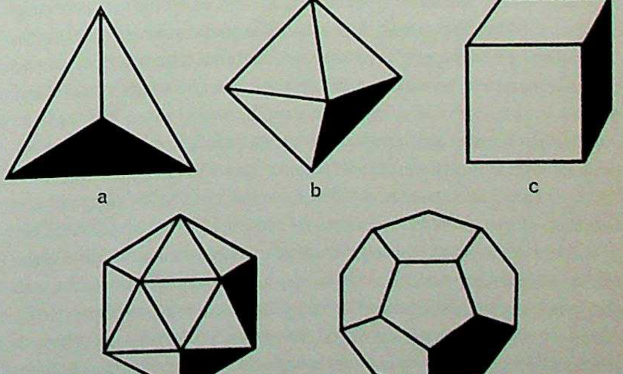

Figure 1 *The five regular solids:* (a) *tetrahedron,* (b) *octahedron,* (c) *cube,* (d) *icosahedron,* (e) *dodecahedron.*

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Was born in 1927 and was educated at Clare College, University of Cambridge, and subsequently worked in biophysical research at the Cavendish Laboratory. He is now on the scientific staff of the British Medical Research Council. His particular interests are in the study, under the electron microscope, of the structure of viruses and the shapes of protein molecules.

The surface detail on virus particles

In 1958 S. Brenner and R. W. Horne described a technique that can show the surface structure of viruses excellently preserved and in high contrast in the electron microscope. They called the technique negative staining. The principle was simply that of drying tiny droplets of a virus suspension containing a small amount of potassium phosphotungstate on a specimen support. The tungstate dries to form a relatively electron-opaque layer in which the virus particles are partly embedded. Their surface structure is imprinted as transparent detail on the dark background. Workers in Cambridge then applied this technique to a preparation of adenovirus. One of their first pictures has become the classical electron microscope picture of a virus (figure 3) [3]. The surface of the adenovirus is shown studded with apparently spherical sub-units about 70 Å apart and regularly arranged to form triangular faces. These faces were clearly part of a perfect icosahedron. On the other hand, the smaller viruses, though they too showed sub-units, looked almost round (figure 4).

The theoretical prediction of surface sub-units

In discussing their pictures of the adenovirus, Horne and his colleagues turned to some predictions about the structure of viruses made earlier by F. H. C. Crick and J. D. Watson [2]. A basic structural requirement of a virus is a shell of protein that can surround and protect the highly specific 'packet' of nucleic acid. Crick and Watson gave the first clear expression to the idea that the protein shell forming the surface of the virus is constructed of identical sub-units, each of which is packed in exactly the same way. X-ray diffraction patterns obtained from crystals of a plant virus had shown that this virus particle possesses cubic symmetry; reasons were given why it was very likely that the protein shells of all the round viruses would also have cubic symmetry. This implies that their surfaces are covered with asymmetrical units—which may be single protein molecules or groups of molecules—each one identically packed with its neighbours and thus each held in place by identical forces. Somewhat unexpectedly, there are only three ways of packing asymmetrical objects symmetrically over a spherical surface, a fact long known to crystallographers. The limitations involved are shown by the problem of writing question marks (asymmetrical objects) on a sphere so that each appears to be surrounded by its neighbours in exactly the same way, no mark being in any way distinguishable from another. In fact, completely symmetrical arrangements can be obtained only when 12, 24, or 60 marks are used. The general solution with 12 points is obtained by superimposing on the sphere a tetrahedron with the same centre (figure 5). Twelve asymmetric marks can then be symmetrically arranged at the points where the sphere cuts the edges of the tetrahedron. The marked sphere has seven axes of symmetry. Four pass from its centre to each of the four vertices of the tetrahedron, because when the sphere rotates about one of these four axes, the surface pattern appears exactly the same three times in each revolution. These four are axes of threefold symmetry. Three axes of twofold symmetry pass through the centres of the opposite edges of the tetrahedron. This arrangement using twelve asymmetrical units is the simplest form of cubic symmetry and is written as (3 2) to identify the nature of the symmetry axes. In a similar way 24 units can be placed on the edges of a cube to cover a spherical surface with (4 3 2) symmetry; the fourfold axes pass through the centres of opposite faces of the cube. The highest form of cubic symmetry requires 60 units placed over a sphere by reference to an icosahedron and gives (5 3 2) symmetry; the fivefold axes pass through each of the six pairs of opposite vertices, at each of which five edges meet.

Crick and Watson argued that if the surface of a virus is made up of identically packed asymmetrical sub-units, then, in general, simple viruses can be only either rod-shaped or approximately round. The round ones should contain either 12, 24, or 60 identical sub-units, packed respectively with (3 2), (4 3 2), or (5 3 2) symmetry to form the outer shell of the virus.

The pictures of the adenovirus obtained by negative staining were in some ways striking confirmation of these predictions; certainly there could be no doubt that the outside of the virus was built of regularly arranged sub-units. However, new problems arose, for there seemed to be clearly six units along each edge of the icosahedron and thus 252 covering the whole surface. Also, although icosahedral arrangements of the virus sub-units was the most likely of the three forms of cubic symmetry, this did not imply that the external shape would be that of an icosahedron. In fact, the arrangement of sub-units seen in the pictures did not suggest cubic symmetry at all unless the units themselves were symmetrical. The twelve units that form the vertices are surrounded by only five neighbours and all the rest by six. Crick and Watson had clearly stated the plausible way in which the round viruses should be built. The fact that apparently they were not put together quite like that was for a time lost sight of, perhaps because of the beauty of the electron-microscope picture of the adenovirus.

Virus antigens

There was other evidence to suggest that viruses might be built of sub-units. In the course of a virus infection, anti-bodies are formed, presumably against some protein component of the virus. But not only virus particles are involved in these reactions; in many cases it was clear that smaller units—so-called soluble antigens—were also reacting with the antibody. In a typical experiment to show this, a gel, such as agar, set in a shallow dish has two small wells cut in it. In one well is placed the anti-serum, in the other a suspension of the antigen. Molecules diffuse out from the wells through the gel, and where the antigen and antibody meet in appropriate concentrations, a line of precipitated material forms. If the antibody is more concentrated or diffuses faster, the line will be nearer the well containing antigen. If there are antibodies against more than one antigen diffusing through the gel, then more than one line will form.

The antigens in preparations of the adenovirus have been studied with this technique by H. G. Pereira and his colleagues [5]. If the antigen well contains a preparation obtained by breaking up tissue-culture cells infected with adenovirus, and the other well anti-serum from an animal previously infected with the same virus, two or more precipitation lines form between the cups. As the adenovirus particles themselves are too large to diffuse through the gel, it seems that during infection of cells with this virus, distinct small antigens are formed in addition to the complete virus itself. The suggestive hypothesis is of course that at least some of these antigens are sub-units from which the virus particles are assembled. The infecting virus can give only a very limited amount of new genetic information to the cell it infects, and it therefore seems unlikely that a lot of new antigens would be produced that had nothing to do with the units required to build the virus. However, although it is tempting to identify the sub-units seen on the virus surface with one or more of the virus antigens detected by immunology, direct proof of this identification has yet to be obtained.

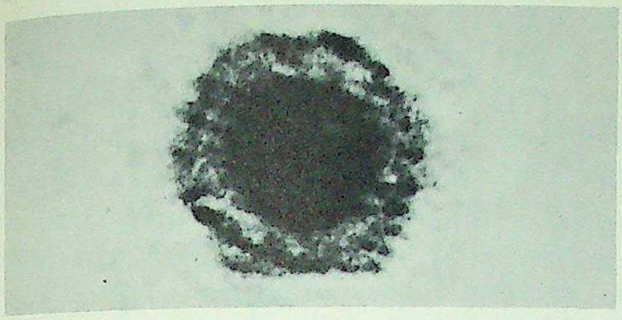

Figure 2 (above) *The adenovirus stained with uranyl acetate. The particle is darkened sufficiently to show a six-sided profile. The dense centre is the core of nucleic acid (DNA) within the outer shell. (× 500 000)*

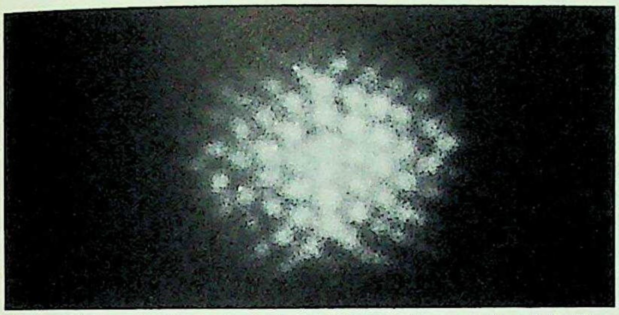

Figure 3 *The adenovirus (700 Å diameter) with negative staining [3]. The array of surface sub-units that form the outer shell of the virus form a perfect icosahedron. (× 500 000)*

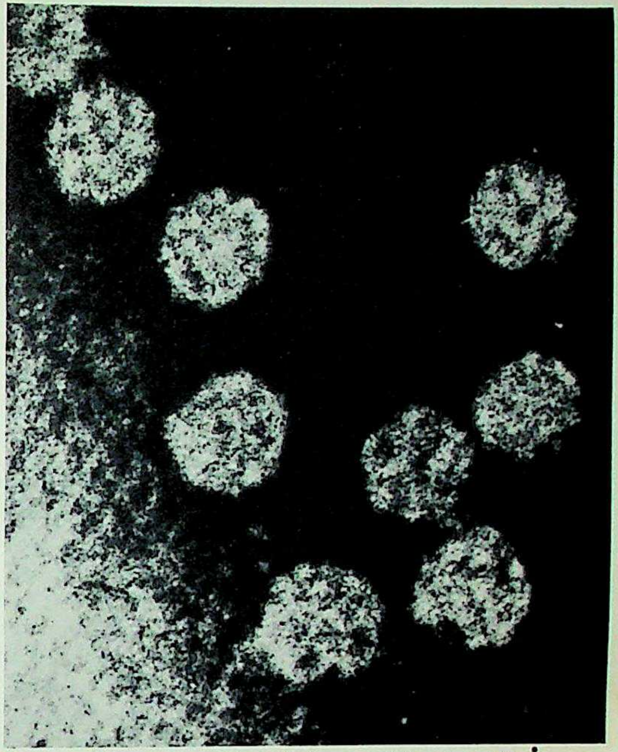

Figure 4 *A small virus (Encephalomyocarditis virus; 270 Å diameter) with negative staining. Sub-units can be detected, but the profile is almost circular. (× 500 000)*

The building of viruses

Recent biochemical work has shown in outline, and also in some detail, how nucleic acid can replicate and direct the formation of specific proteins. It is therefore possible to understand, at least in general terms, how the components of a virus are formed in an infected cell. These components then come together to form the virus particles with a unique size and shape that is revealed by electron microscopy. Something, it seems, that predetermines what the virus will be like is built into the sub-units and prevents them from forming into objects of any other appearance.

One suggestion of the way in which virus formation is determined came from R. W. Horne and P. Wildy [4]. Their idea is that the sub-units that form the surface are not the asymmetrical units proposed by Crick and Watson, but symmetrical units of two kinds, one having sixfold symmetry, the other fivefold. As a matter of geometry, only units with fivefold symmetry can lie on the axes of fivefold symmetry without making the assembly asymmetrical. In the adenovirus, their position would be on the twelve vertices of the icosahedron. The units with sixfold symmetry pack together well, each with six neighbours, and could lie on axes of twofold or threefold symmetry without destroying the symmetry of the surface. Any other unit in such a position would destroy this. These units, packed as suggested by the electron micrograph, would give the adenovirus icosahedral symmetry. A difficulty with this account of virus structure is that it does not explain the icosahedral shape of the adenovirus or the uniform size of virus particles in general. If an edge of the adenovirus consists of six units—a unit of fivefold symmetry at each end with four units of sixfold symmetry in between—it is hard to understand why particles never form with five or seven units on an edge. These would obviously be different in size. They are in fact never found. In the case of the larger *Tipula* Iridescent Virus, it is even harder to understand how the size of the virus is determined. The core of nucleic acid does not seem to be the determining factor, for the particles deficient in nucleic acid that sometimes occur still have the same characteristic size.

An account of how the shell of a virus is constructed was put forward by A. Klug and D. L. D. Caspar in a review of the data on virus structure obtained from X-ray diffraction [6]. They suggested that the sub-units seen by electron microscopy were not true building units, but positions where still smaller asymmetrical crystallographical units happen to lie close together and are seen as one. This explanation found little favour with electron microscopists, who were naturally reluctant to abandon their solid-looking sub-units just because they did not fit with crystallographic concepts. Caspar and Klug have now put forward a new theory [1] that allows electron microscopists their sub-units as the morphological units. But the theory is based on the idea that the shell is built up of smaller structural units that are arranged with only slight departures from crystallographic geometrical perfection. More important, the theory does suggest how the size and shape of virus particles are determined.

The arguments behind these new ideas are complex, but a précis may do them partial justice. The original idea of Crick and Watson was that each sub-unit would be identically situated with respect to its neighbours so that exactly similar bonds hold each unit in position. However, complete equivalence is possible only when there are 12, 24, or 60 units on the surface, and this does not fit with what has since been seen by electron microscopy. Caspar and Klug now suggest that the basic hypothesis should be modified by allowing a small amount of deformation, up to 5 degrees, of the bonds between sub-units. The sub-units then need not be in perfect equivalence. The problem becomes one of finding a pattern in which to arrange points different in number from 12, 24, or 60 over

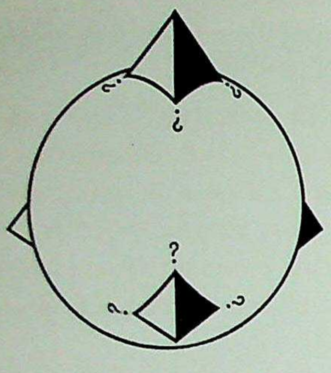

Figure 5 *Twelve asymmetrical units can be arranged on the surface of a sphere in perfect symmetry at the points where the sphere is intersected by a concentric tetrahedron. The arrangement has tetrahedral (3 2) cubic symmetry (see text).*

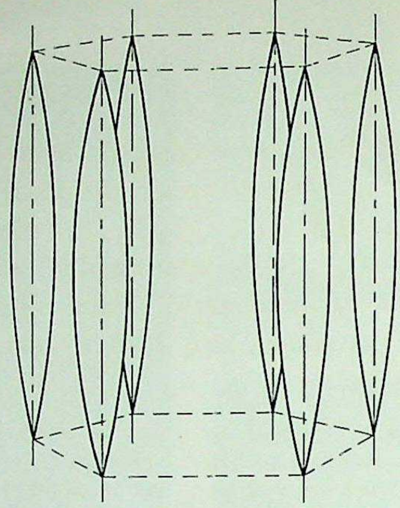

Figure 6 *The building of a morphological sub-unit from six basic building units as suggested by Caspar and Klug [1].*

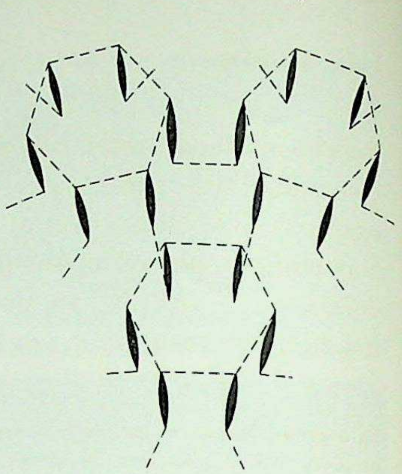

Figure 7 *The generation of a curved surface by the inclination of the bonds.*

the surface of a sphere so that each is very nearly identically related to its neighbours. It is shown that this can be done with certain multiples of 60 points.

The process of virus formation is now pictured in this way. The cell, in response to the information conveyed by the nucleic acid of the infecting virus, produces large numbers of identical protein molecules that form the basic building units. These are supposed to be roughly cigar-shaped; this is known to be true in one case, though in general the shape is not known. The molecular weight is assumed to be about 20 000—rather too small to distinguish with the electron microscope. In a particularly relevant example, these basic units are considered to unite together by specific chemical bonds into groups of six (figure 6), rather like a bundle of six cigars. It is these groups, and not the basic structural units, that are considered to be the morphological sub-units seen with the electron microscope. The groups can then combine together by further bonds to form a hexagonal pattern; the important feature of this array is that every basic unit is identically linked to its neighbours by the same chemical bonds. This is possible because each is in an exactly equivalent position. Such an arrangement would go on forming a flat layer, one 'cigar' thick, until the supply of basic units ran out. However, this picture of surface formation has assumed that the bonds between units are so directed that the axes of all the groups of six units are parallel and upright. If the bonds were in fact inclined to each other at a small angle (figure 7), the result would be different: as the groups started to bond together, a curved surface would begin to form. However, as a matter of geometry it is not possible to continue the process very far with each group having six neighbours. It soon becomes impossible to add further units at anything like the required angles: further aggregation then stops. But the situation is at once eased if a group containing five basic units instead of six is introduced and surrounded by only five neighbours. The deformation of bond angles required to do this is only small. Growth of the surface can then continue until another five-neighbour unit is needed. The most stable arrangement leads to a closed shell when twelve five-neighbour groups are introduced symmetrically. If the hexagonally packed areas in between them are nearly flat, the resulting surface is almost an icosahedron with the five-unit groups at the vertices; this is exactly the arrangement shown by the adenovirus (figure 3).

It is clear that the bond angles between the basic building units can thus exactly predetermine the extent to which hexagonal packing continues before a five-unit group is the only sort that can fit into place. The distance between vertices is thus exactly fixed, and the basic units can build a virus only of a precisely determined size. The total number of groups —that is, of sub-units as seen by electron microscopy—that go to form the surface of a virus built in this way must conform with the equation

$$M = 10Pf^2 + 2$$

where M is the number of morphological sub-units, $P = 1$ or 3, and $f = 1, 2, 3, 4, \ldots$ The picture of the adenovirus (figure 3) suggests that for this virus $M = 252$ (deduced from the presence of six units along each edge). This number is given by $P = 1$, $f = 5$.

When the alignment of the morphological groups is nearly parallel, large nearly flat areas form the faces of the virus, which will therefore be relatively large and nearly an icosahedron (figure 3). A marked inclination of the groups leads to a small virus that should look nearly round (figure 4).

The theoretical ideas of Caspar and Klug give a fundamental explanation of the more empirical concepts of Horne and Wildy. Both leave unsolved the problem of how the nucleic acid is arranged inside the shell. And there are still many problems relating to the more complex viruses, such as those of the influenza and pox groups; these viruses, in addition to their specific nucleoprotein, which appears to be a folded rod-like structure, also transform and incorporate parts of the host-cell. As yet there is nothing like an understanding of how the more complicated viruses form.

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The aromatic fluorocarbons and their derivatives

J. C. Tatlow

Recent synthetic work has made many new aromatic fluorocarbons available. These can be converted into various derivatives with different functional groups—hexafluorobenzene, for example, gives derivatives of general formula $C_6F_5.X$. The directional effects that operate when a pentafluorophenyl compound ($C_6F_5.X$) is substituted a second time to give a difunctional derivative ($Y.C_6F_4.X$) are now being investigated. These new fluorine compounds are interesting in their own right, and, in addition, may lead to materials of commercial significance.

In organic chemistry, the element second in importance to carbon itself is hydrogen. Most organic materials contain appreciable numbers of hydrogen atoms. When first studying the subject it is usual to consider the various classes of functional groups as replacing hydrogen atoms in hydrocarbon structures. Though substituents involving other elements may be dominant in influencing properties of a compound, nevertheless some hydrocarbon character is retained in most cases.

Organic fluorine chemistry is now well established, and it is generally recognized that fluorine also occupies a special place in organic chemistry. It is not merely another substituent, but an element that can give rise to a whole system of organic compounds, just as hydrogen can. Like hydrogen, it is univalent and its atomic size is such that there is room round a carbon chain for all the atoms that can be bonded to carbon. However, the atomic size of fluorine is greater than that of hydrogen. Hence, in a chain of $\rangle CF_2$ units the carbon skeleton is well protected, and since the C—F bond is a very strong one, saturated fluorocarbons are very stable chemically. They are non-inflammable and have virtually no synthetic uses. By indirect means, however, various atoms and functional groups can be joined to fluorocarbon chains or rings, giving rise to the whole range of inter-related families of compounds typical of organic chemistry. Further, carbon skeletons can carry hydrogen and fluorine substituents indiscriminately, with or without functional groups being present as well. It seems unlikely that other elements besides hydrogen and fluorine will give rise to such extensive systems of organic chemistry. Chlorine, for instance, forms a bond with carbon less stable than that from fluorine, and its atomic radius is greater, so that chlorocarbon chemistry is more limited than fluorocarbon chemistry. However, all types of chlorofluorocarbon structures are possible, and the presence of fluorine atoms not only limits the steric strain arising from the big chlorine atoms, but stabilizes the carbon-chlorine bonds in the vicinity. Thus, vast numbers of organic compounds containing carbon, fluorine, and functional groups, and mixed systems with carbon, fluorine, hydrogen, and chlorine for example, are possible. These compounds have many properties different from those of general organic chemistry, but they are obviously organic in character, and are related to hydrocarbon analogues.

Most of the developments in fluorocarbon chemistry have been with aliphatic compounds. As indicated above, chemical inertness is associated with a fluorocarbon chain, but most functional groups have characteristic reactions, though these may be modified considerably compared with hydrocarbon chemistry. Fluorocarbon derivatives show many unusual physical properties; for example, many have poor solubilities in hydrocarbon derivatives.

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Was born in 1923 and was educated at Rugeley Grammar School and the University of Birmingham. After a period as Scientific Officer in the Ministry of Supply on the atomic energy project he returned to the University of Birmingham as a Lecturer, Senior Lecturer, and then Reader in organic chemistry, being appointed Professor of Organic Chemistry in 1959. His particular research interest is in the organic chemistry of fluorine compounds.

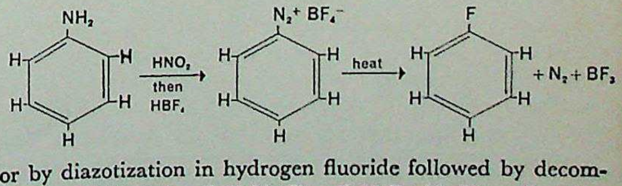
Industrial development has followed research in aliphatic fluorine chemistry [1]. Many specialist materials are now readily available, the general properties outlined above being worth the relatively high cost. One of the most important is the I.C.I. non-inflammable anaesthetic Fluothane ($CF_3CHClBr$). In the polymer field, polytetrafluoroethylene (Teflon, Fluon) is well known. It has chemical inertness and is relatively stable to heat. These properties are accompanied by other useful features, such as incompatibility with all solvents, and the formation of a surface with low coefficients of friction with many materials, and to which few things will adhere. Other fluoropolymers show these properties in less extreme form. Water-resistant films, surface coatings, and rubbers have been developed.

In terms of quantity, the most important fluorochemicals are the simple chlorofluorocarbons (e.g. CCl_2F_2, $CHClF_2$, $C_2Cl_2F_4$), used extensively as working fluids in compression refrigerators and air-conditioners and as propellants in aerosol-pressurized packaging so popular in recent years. Other uses of these materials are as blowing agents for plastic foams and as gas springs for vehicles. Fluorochemicals have also found application as fire extinguishers and stable surface-active agents.

Some aromatic fluorocompounds have been known for some time. Examples are derivatives of benzene, naphthalene, or diphenyl containing one or two fluorine atoms. However, no fully fluorinated aromatic compounds have been prepared until relatively recently. A whole range has now become available and a new section of organic chemistry has opened up. The purpose of this article is to summarize these developments.

Synthetic routes to aromatic fluorides

The standard route [2*a*] to aryl fluorides has been through diazonium compounds, either by converting a diazotized amine into the diazonium borofluoride followed by heating:



or by diazotization in hydrogen fluoride followed by decomposition: $C_6H_5NH_2 \rightarrow C_6H_5N_2^+F^- \rightarrow C_6H_5F + N_2$. These fluorides can be nitrated and reduced to give amines, to which the conversion can be applied again. However, long sequences are required to give highly fluorinated compounds, and full fluorination, to give, for example, hexafluorobenzene, has never been achieved. Other standard fluorination techniques have been applied to aromatic compounds [2*b*]. A possible approach is halogen exchange, such as the reaction of hexachlorobenzene with potassium fluoride in a suitable solvent. Though syntheses of fully fluorinated aromatic compounds in this way have not been reported so far, they may become possible. Certainly, many partly fluorinated aromatics can now be made thus. Direct replacement of hydrogen by fluorine, in benzene for example, has proved impossible. Agents for exhaustive fluorination, including the element itself and high-valency transition metal fluorides, such as cobaltic fluoride, give alicyclic polyfluorides —C_6F_{12}, C_6HF_{11}—as the aromatic ring is readily saturated.

Syntheses of highly fluorinated aromatics

Two practicable routes to highly fluorinated aryl derivatives have recently been found. One involves pyrolysis of simple aliphatic fluorides; the most useful example so far is the preparation of hexafluorobenzene by heating tribromofluoromethane [3].

The second route starts from an aromatic hydrocarbon. This is fluorinated exhaustively, usually, though not invariably, with cobaltic fluoride [4].

There are two possible reactions; in one, the hydrogen is only partially replaced. From benzene, polyfluorocyclohexanes $C_6H_nF_{12-n}$ ($n = 1, 2, 3,$ or 4) are obtained. Aromatic unsaturation is then re-created by elimination of hydrogen fluoride with alkaline reagents [5], or by passage over a heated metal fluoride (figures 1 and 2).

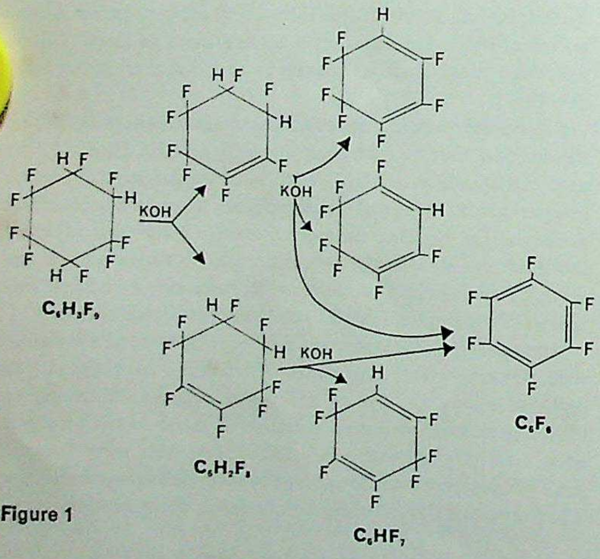


Figure 1

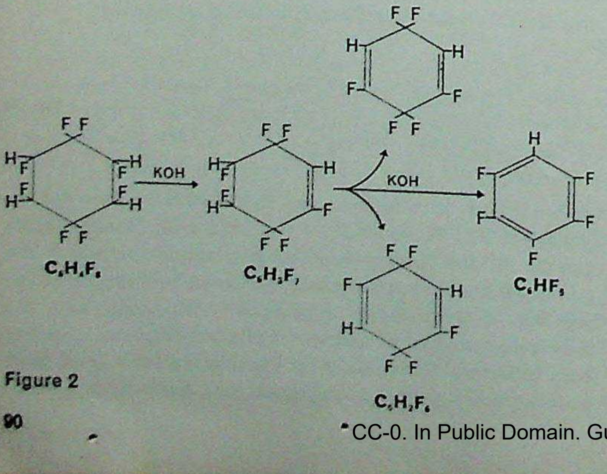


Figure 2

In the second type of reaction, aromatization is effected by elimination of fluorine as a metallic fluoride by passage over heated metals such as iron or nickel [6]. Alicyclic fluorides that can be converted into aromatic compounds of the same ring size include olefins and diolefins; examples are the octafluorocyclohexadienes made from decafluorocyclohexanes (figure 3). Saturated fluorocarbons, made readily [2*b*, 4] by complete fluorination of hydrocarbons, can also be defluorinated (figure 4). Though the reaction probably goes stepwise, only the aromatic compound is formed in reasonable yield. Polycyclic aromatic fluorocarbons made thus include perfluoronaphthalene, perfluoroacenaphthylene, and perfluoropyrene. Perfluorostyrene and pentafluoropyridine have also been prepared.

Pentafluorophenyl derivatives from pentafluorobenzene

As various polyfluoro-aromatics became available, reactions were carried out on them to ascertain their possible uses in

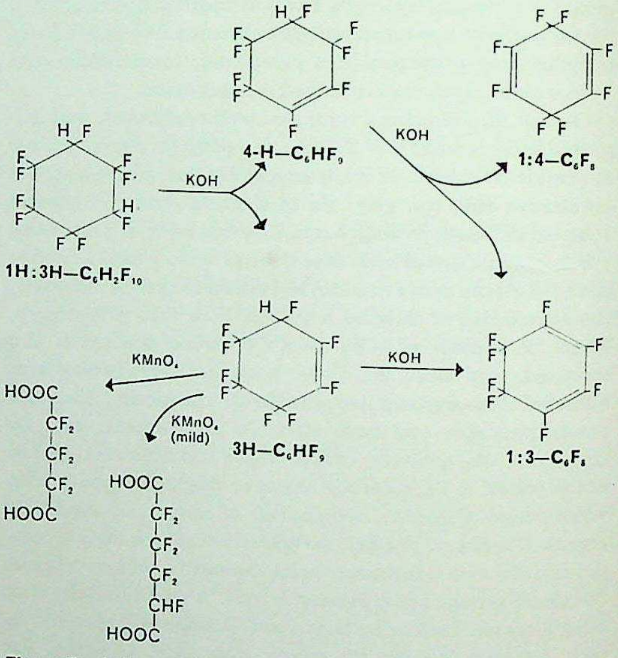


Figure 3 *Action of alkali on $1H{:}3H\text{—}C_6H_2F_{10}$*

syntheses. The simplest approach was to carry out some standard electrophilic replacements of hydrocarbon aromatic chemistry, using positive reagents, or those that behave as such, on the hydrogen of pentafluorobenzene. This worked successfully with sulphuric acid to give pentafluorobenzenesulphonic acid, while with the appropriate halogen in sulphuric acid, bromo- or iodopentafluorobenzene was made [7]. The last two are valuable synthetic intermediates, since they react with copper to give decafluorodiphenyl, and with magnesium readily form the appropriate Grignard reagents. These reagents can be converted into a wide range of derivatives containing the pentafluorophenyl group, including pentafluorobenzaldehyde and various alcohols and ketones (figure 5). It seems that pentafluorophenyl magnesium halides undergo the usual extensive range of reactions that are typical of Grignard reagents [7, 8]. The primary products of these reactions have been converted by orthodox reactions into various other pentafluorophenyl derivatives. For example, pentafluorobenzaldehyde undergoes classical reactions (figure 6).

Bromopentafluorobenzene forms pentafluorophenyl lithium with lithium amalgam [9]. This will behave similarly to the

Grignard reagent in many standard syntheses. It will also act as a source of transitional tetrafluorobenzyne in some reactions. For example, addition of bromine to pentafluorophenyl lithium in diethyl ether gave largely bromopentafluorobenzene, but the product contained some 1,2-dibromotetrafluorobenzene. If pentafluorophenyl lithium was made in furan as solvent, 1,2,3,4-tetrafluoro-5,8-dihydro-5,8-endoxonaphthalene was formed. This could be converted into 1,2,3,4-tetrafluoronaphthalene.

Displacement of fluorine from hexafluorobenzene by nucleophilic reagents

In general, fluorine atoms in highly fluorinated aromatic compounds can be replaced by nucleophilic reagents, those with negative charges ($\overline{O}CH_3$, $\overline{S}H$, $\overline{O}H$, $\overline{C}H_3$) or with lone pairs of electrons ($:NH_3$, $:NH_2—NH_2$, $:NH_2.CH_3$). There is thus a general route to aryl fluorocarbon derivatives that is parallel to the standard electrophilic replacements of hydrocarbon aromatic chemistry, but involves opposite charges (F^- displaced by X^-, H^+ displaced by Z^+). Various pentafluorophenyl derivatives have been made in this way from hexafluorobenzene, giving a second synthetic approach to compounds of this type [10–12] (figure 7).

The functional groups so introduced can be further treated to give other new pentafluorophenyl derivatives, using the standard reactions of organic chemistry. Thus, pentafluorophenol (C_6F_5OH) was made from pentafluoroanisole ($C_6F_5OCH_3$). The amino-group of pentafluoroaniline ($C_6F_5NH_2$) showed characteristic reactions, it can, for example, be acylated and diazotized.

Pentafluorothiophenol ($C_6F_5.SH$) lost its sulphur and was converted to pentafluorobenzene by reaction with Raney nickel. This is a useful general reaction for these thiophenols that will be discussed later. Pentafluorothiophenol is a useful starting point for making many sulphur compounds. It was methylated with diazomethane, and the resulting

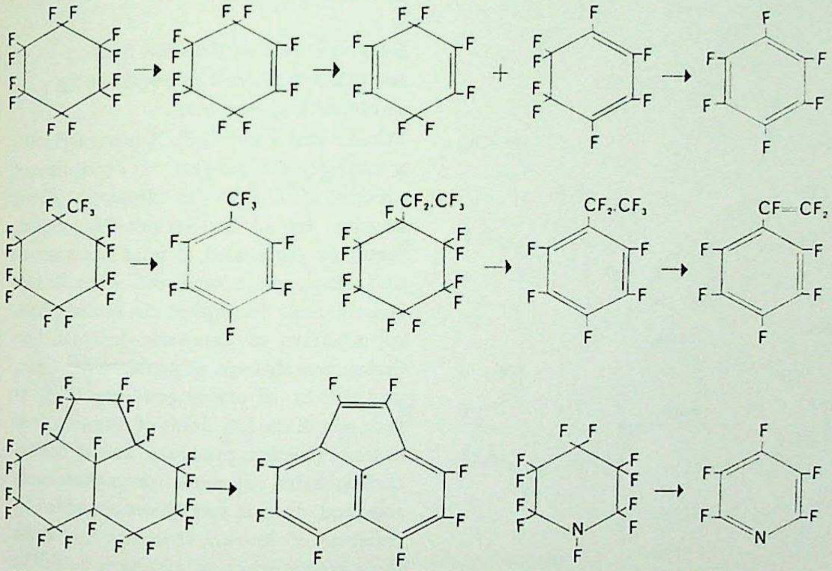


Figure 4 *Synthesis of aromatic fluorocarbons by defluorination*

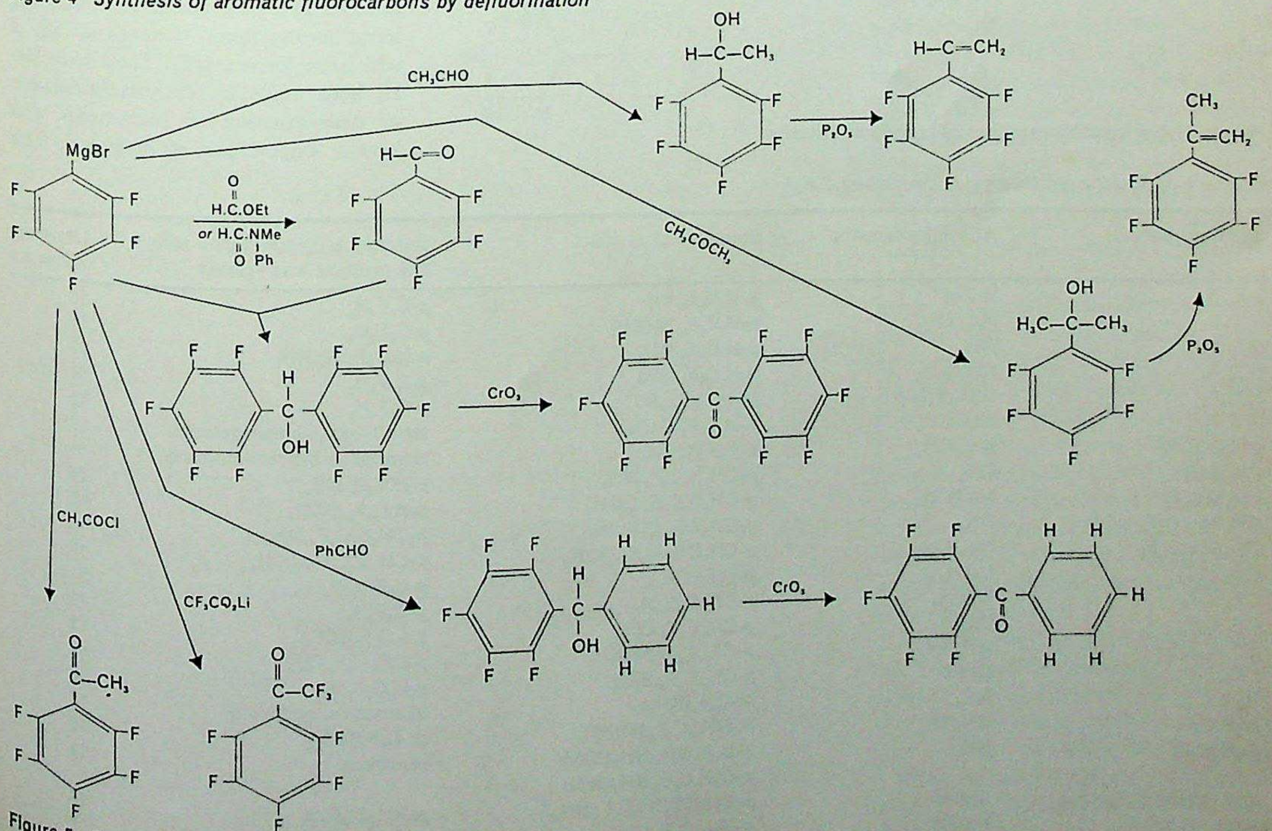


Figure 5 *Syntheses from pentafluorophenyl magnesium halides*

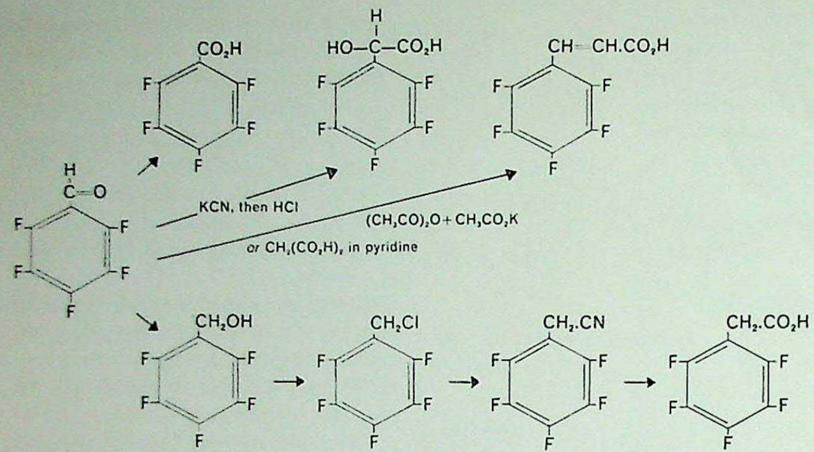


Figure 6 *Reactions of pentafluorobenzaldehyde*

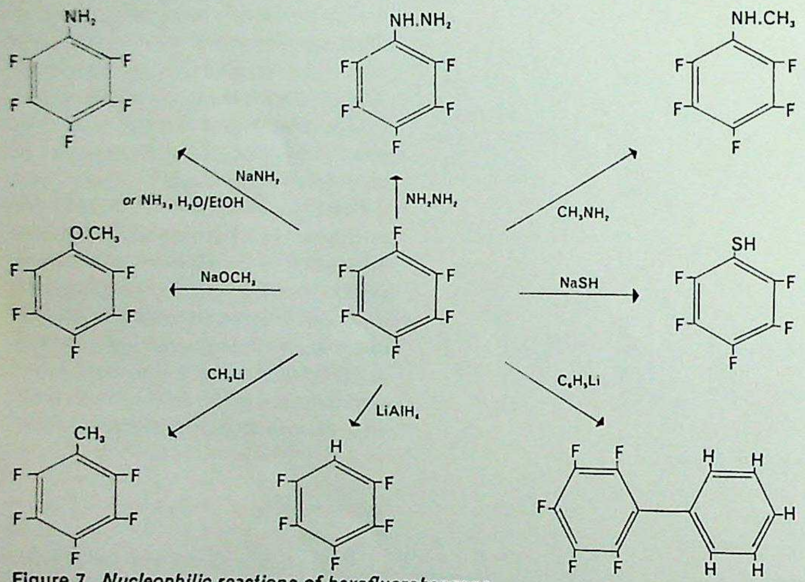


Figure 7 *Nucleophilic reactions of hexafluorobenzene*

sulphide ($C_6F_5.S.CH_3$) oxidized to methyl pentafluorophenyl sulphone

$$(C_6F_5.SO_2.CH_3)$$

Oxidation of pentafluorothiophenol with chlorine and hydrogen peroxide in acetic acid gave pentafluorobenzenesulphonyl chloride ($C_6F_5.SO_2Cl$), which was converted in the usual way into sulphonate esters and sulphonamides. Many pentafluorophenyl derivatives containing a range of functional groups are thus available, and will undergo many of the standard reactions of aromatic chemistry [17].

Displacement of fluorine from pentafluorophenyl derivatives by nucleophilic reagents

When a derivative $C_6F_5.X$ is treated with a nucleophilic reagent, a disubstituted product ($Y.C_6F_4.X$) is obtained. Three isomers are of course possible, ortho, meta, or para, and it is of interest to find which are formed and what factors control their formation. In electrophilic substitution of aromatic hydrocarbon derivatives this sort of problem has been, and still is, of major concern: it is, in fact, one of the big fields of research into organic reaction processes. In the fluorocarbon series, reference compounds were required, that is tetrafluorobenzene derivatives of known structure to which the various reaction products could be related. The most useful have been the tetrafluorobenzenes themselves, all of which are known [13]. They have also all been made by dehydrofluorination or defluorination of compounds with known dispositions of hydrogen. This

Products of fluorine replacement in derivatives C_6F_5X

Starting material	Attacking reagent	Structure of product	Reference compound to which the product was related	Literature reference
$H.C_6F_5$	NaSH	p-$H.C_6F_4.SH$	p-$C_6F_4H_2$	10
$H.C_6F_5$	NH_2NH_2	p-$H.C_6F_4.NHNH_2$	p-$C_6F_4H_2$	11
$H.C_6F_5$	NH_3	p-$H.C_6F_4.NH_2$	p-$H.C_6F_4.NHNH_2$	11
$H.C_6F_5$	KSPh	p-$H.C_6F_4.SPh$	p-$C_6F_4H_2$	10
$H.C_6F_5$	KSC_6F_4H-p	$(p\text{-}H.C_6F_4)_2S$	p-$C_6F_4H_2$	15
$H.C_6F_5$	$NaOCH_3$	p-$H.C_6F_4.OCH_3$	tetrafluoro-*p*-benzoquinone	15
$CH_3O.C_6F_5$	$NaOCH_3$	p-$C_6F_4(OCH_3)_2$	tetrafluoro-*p*-benzoquinone	14
$CH_3S.C_6F_5$	NH_3	p-$CH_3S.C_6F_4.NH_2$	p-$H.C_6F_4.NH_2$	15
$CH_3S.C_6F_5$	$NaOCH_3$	p-$CH_3S.C_6F_4.OCH_3$	p-$H.C_6F_4.OCH_3$	15
$CH_3SO_2.C_6F_5$	NH_3	p-$CH_3SO_2.C_6F_4.NH_2$	p-$CH_3S.C_6F_4.NH_2$	15
$CH_3SO_2.C_6F_5$	$NaOCH_3$	p-$CH_3SO_2.C_6F_4.OCH_3$	p-$CH_3S.C_6F_4.OCH_3$	15
$CH_3.C_6F_5$	$LiCH_3$	p-$C_6F_4(CH_3)_2$	p-$C_6F_4(CO_2H)_2$	7
$CF_3.C_6F_5$	$LiAlH_4$	p-$CF_3.C_6F_4.H$	p-$C_6F_4H_2$	12
$CF_3.C_6F_5$	$LiCH_3$	p-$CF_3.C_6F_4.CH_3$	1,4-$C_6F_{10}(CF_3)_2$	12
$CF_3.C_6F_5$	NH_2NH_2	p-$CF_3.C_6F_4.NHNH_2$	p-$CF_3.C_6F_4.H$	12
$CF_3.C_6F_5$	KSPh	p-$CF_3.C_6F_4.SPh$	p-$H.C_6F_4.SO_2Ph$	12
$H_2N.C_6F_5$	NH_3	m-$C_6F_4(NH_2)_2$	alternative synthesis	11
$H_2N.C_6F_5$	NH_2NH_2	m-$NH_2.C_6F_4.NHNH_2$	m-$C_6F_4(NH_2)_2$	15
$O_2N.C_6F_5$	NH_3	o-$O_2N.C_6F_4.NH_2$(70%) p-$O_2N.C_6F_4.NH_2$(30%)	reactions	11
$CH_3CONH.C_6F_5$	NaSH	p-$CH_3CONH.C_6F_4.SH$	p-$NH_2.C_6F_4.H$	15
$\frac{1}{2}SO_4^{=}N_2^{+}.C_6F_5$	NaOH	p-$NH_2.C_6F_4.OH$	tetrafluoro-*p*-benzoquinone	15

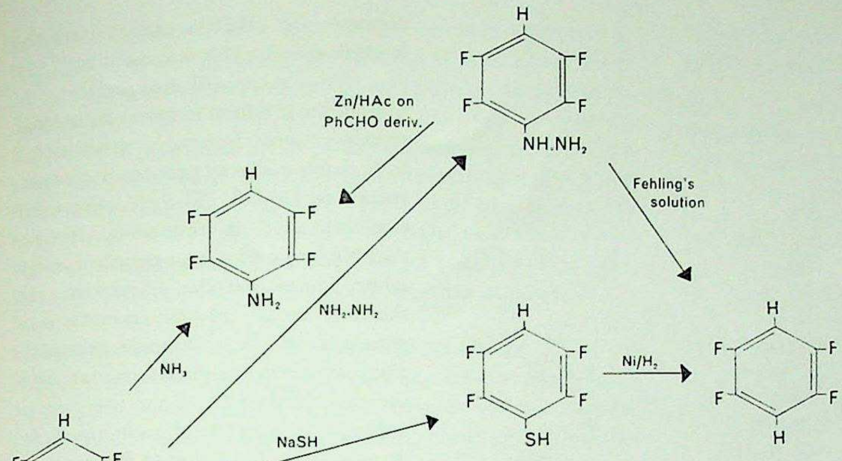


Figure 8 *Nucleophilic replacements on pentafluorobenzene*

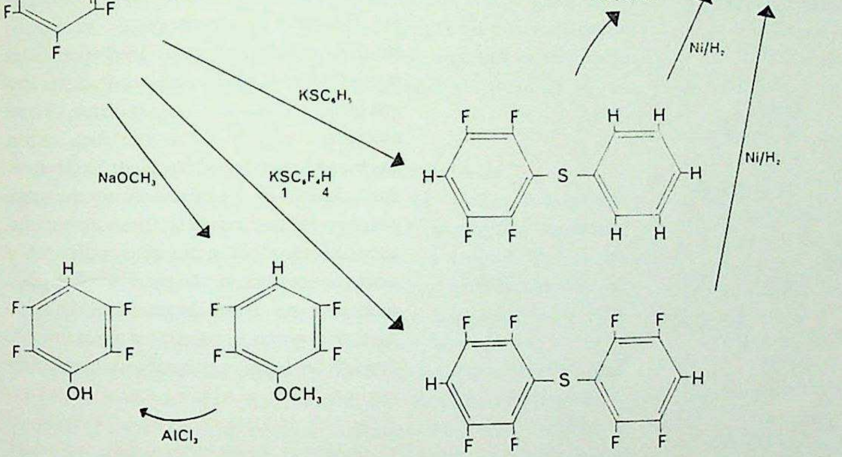


Figure 9

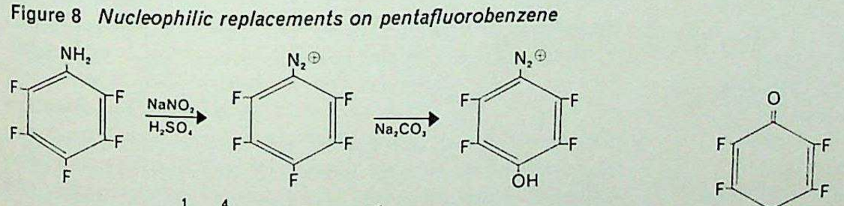
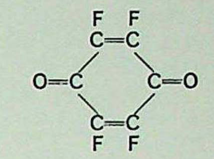


Figure 10 *Reactions of pentafluorotoluene*

made it possible to confirm their structures [6]. Another reference compound is tetrafluoro-*p*-benzoquinone



prepared by hydrolysis of the $\rangle CF_2$ groups of octafluorocyclohexa-1,4-diene with sulphuric acid [14].

A number of pentafluorophenyl derivatives have been subjected to further nucleophilic attack, and the products orientated by relating them to reference compounds of known structure. The results are summarized in the table on page 92. The structures of the products have been confirmed in all cases by nuclear magnetic resonance spectroscopy.

The orientations of the products from pentafluorobenzene are summarized in figure 8, the 1,2,4,5-tetrafluorobenzene formed from each reaction being identical with an authentic specimen. The methoxy group was also introduced para to the hydrogen, since the tetrafluorophenol was identical with the product formed from the aminophenol derived from the diazonium salt (figure 9). This aminophenol could be shown to have nitrogen and oxygen arranged para to each other, as oxidation gave tetrafluoro-*p*-benzoquinone. Reduction of this quinone followed by methylation afforded tetrafluoro-*p*-dimethoxybenzene, and an identical product was formed by reaction of pentafluoroanisole ($C_6F_5.OCH_3$) with sodium methoxide. Both reactions on methyl pentafluorophenyl sulphide gave para-orientated products, since each had its methyl sulphide grouping replaced by hydrogen on reaction with nickel-hydrogen to give the corresponding tetrafluorobenzene derivative made earlier. These primary products (*p*-$CH_3S.C_6F_4.NH_2$ and *p*-$CH_3S.C_6F_4.OCH_3$) could be oxidized to the corresponding derivatives with sulphone (SO_2) groups. These compounds were identical with those obtained by direct replacement reactions on the sulphone $CH_3SO_2.C_6F_5$. The orientations of the products from penta- and octafluorotoluene are summarized in figures 10 and 11.

Pentafluoroaniline gave meta-orientated disubstitution products. The meta-diamine was synthesized also from an alicyclic precursor in which the nitrogens were arranged on carbon atoms 1 and 3.

While the major part of the product in each case discussed has the structure given, it might be expected that minor amounts of other isomers would be formed as well. This was confirmed with pentafluorobenzene in two reactions; the ratio of the products formed was approximately 5 ortho : 1 meta : 94 para [11].

It is too early to propose a complete theory to explain all these effects, but some observations are possible. It seems that the reagent used has only a minor effect, if any, on the orientation, and that the nature of the aromatic compound is important. It seems reasonable also that in compounds of formula $C_6F_5.X$ the electronic effects of the five fluorine atoms will together be far more significant in most cases than that of the group X.

The electronic effects usually assumed for fluorine in electrophilic reactions, that is, replacements of hydrogen from monofluorobenzene, are an inductive attraction that withdraws some of the electronic charge from the ring and a back-conjugation which feeds back negative charge predominantly to the para position of the ring. If these effects are ascribed to all five fluorine atoms of a pentafluorophenyl derivative ($C_6F_5.X$), assuming no effect from X, it follows that the position para to the group X should be most susceptible to attack by

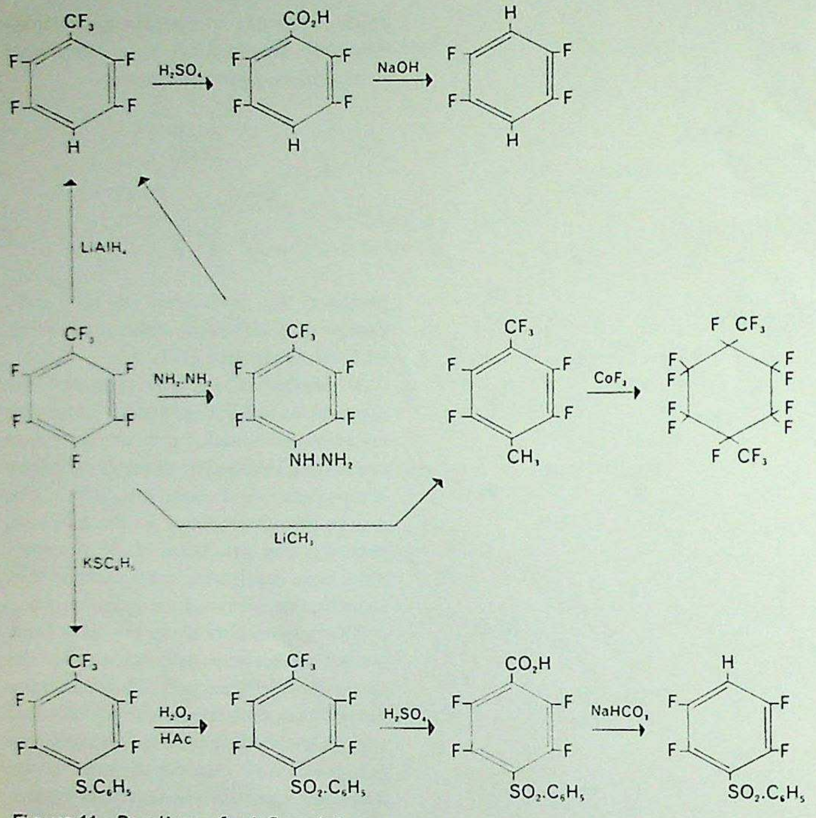

H₂SO₄
NaOH
LiAlH₄
NH₂.NH₂
CoF₃
LiCH₃
KSC₆H₅
H₂O₂
HAc
H₂SO₄
NaHCO₃

Figure 11 *Reactions of octafluorotoluene*

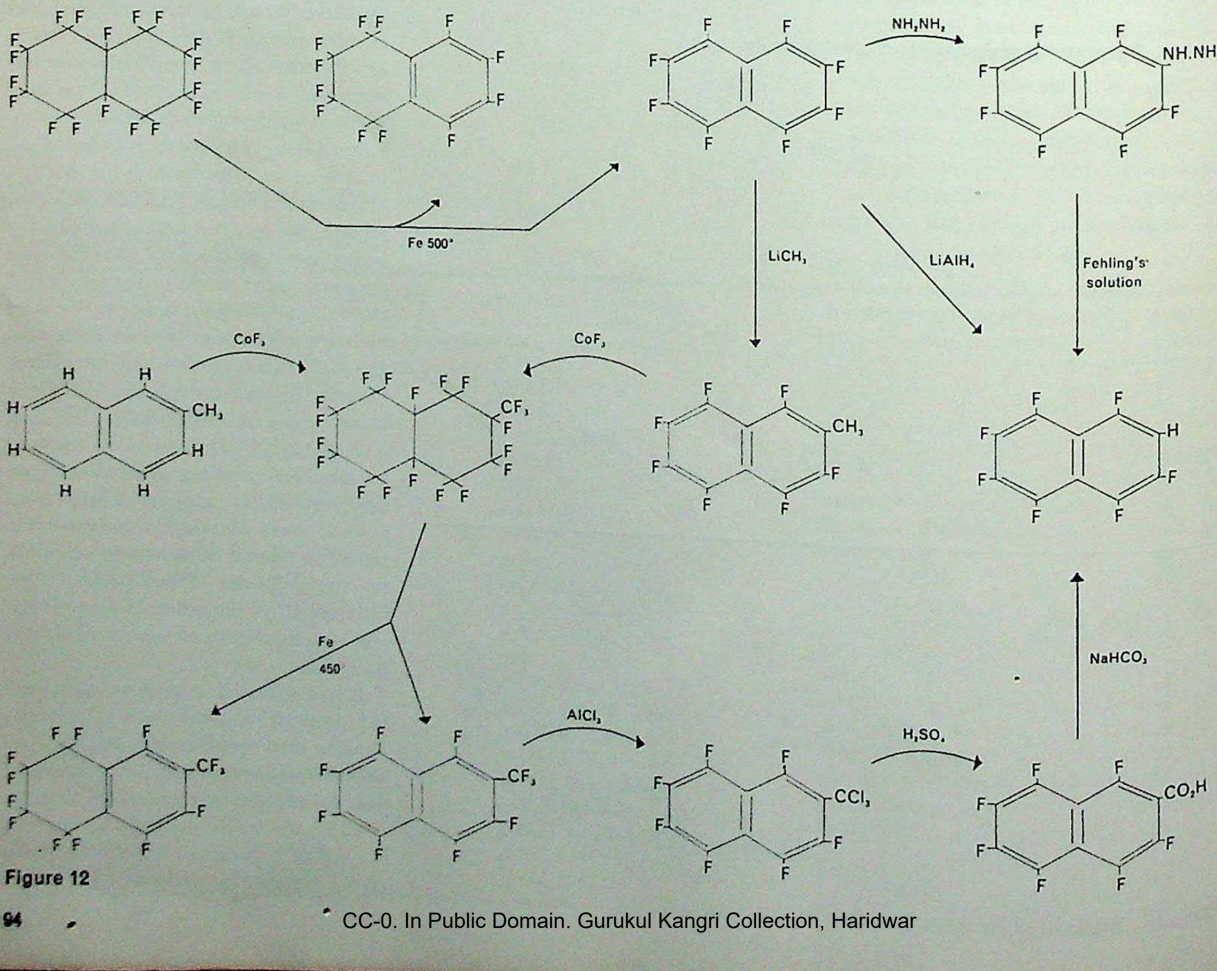

NH₂NH₂
Fe 500°
LiCH₃
LiAlH₄
Fehling's solution
CoF₃
CoF₃
Fe 450°
AlCl₃
H₂SO₄
NaHCO₃

Figure 12

negative species. If X is only weakly electron attracting or repelling, as are most groups, the reaction rates will be affected, but not the position of attack. Powerful electronic attraction, for example by the nitro group, will assist replacement not only of the para fluorine but of the ortho one as well, and the reaction is very rapid. Powerful repulsion of electrons by a group such as the amino group, which has a lone pair of electrons capable of back-conjugation into the ring, will make attack difficult. It will deactivate the ortho and para positions most, so that the first replacement goes in the meta position.

Reactions of polycyclic aromatic fluorocarbons

Though most work in the field has so far been carried out in the hexafluorobenzene series, more complex aromatic fluorocarbons offer much scope for interesting chemistry. One series of reactions on octafluoronaphthalene is summarized in figure 12 [16]. It will be seen that the fluorine in the β position is replaced preferentially in the first attack by nucleophilic reagents. This was demonstrated by relating the products to perfluoro(2-methyldecalin), the fluorination product of 2-methylnaphthalene.

Physical properties of aromatic fluorocarbons

The elementary physical properties of perfluoro-aromatic compounds resemble closely those of analogous aromatic hydrocarbon derivatives. For example, the melting points are often similar. In their solution properties, perfluoro-aromatic compounds do not show those extremes of abnormality that characterize perfluoro-aliphatic compounds, and they seem to occupy a position intermediate between the latter and normal organic compounds. For example, hexafluorobenzene is miscible with normal organic solvents and with perfluoromethylcyclohexane. Complexes are formed in mixtures of aromatic hydrocarbons and perfluoro-aromatic compounds. Thus, one exists between benzene and hexafluorobenzene.

Future work in the field

There is unlimited scope for further work in this new field of organic chemistry. On the research side, much synthetic work remains to be done to extend the range of available compounds and to find new reactions of the series. Also, the detailed pattern of nucleophilic substitution needs to be established and the mechanisms elucidated.

It is also certain that there will be many attempts to find commercial outlets for materials based on aromatic fluorocarbons in the next few years. The search has already started in applications in which materials based on hydrocarbon-type aromatic derivatives are used. Examples are dyestuffs, polymers, and biologically active compounds. Dyestuffs based on perfluoroaryl systems could well show new colours and good resistance to fading. Polymers should show the good heat and radiation stability typical of aromatic systems and possibilities for obtaining various physical forms. In the area of medicinal and agricultural chemicals there is vast scope for making fluoro analogues of biologically active compounds. It is not yet possible to say whether an industrial chemistry will be based on aromatic fluorocarbons, let alone whether it will involve such uses. It does seem likely that the fluorination of organic compounds will always be expensive. Accordingly, there will be a delicate balance between special properties and the extra cost to the consumer of the materials possessing them.

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The role of interferon

Alick Isaacs

The attack of a virus on an organism is resisted in a number of ways—the organism develops antibodies, for example. It has recently been discovered that the cells of vertebrates produce a substance that interferes with the replication of the virus. This substance, interferon, seems to assist the organism to resist and to recover from virus infections. This article discusses the action of interferon, both in infected cells, where it seems to act as a 'regulator', and in normal cells.

Interferon is the name that was given to an antiviral substance that is produced by vertebrate cells in response to virus infection. Its interest lies in the fact that it is a naturally occurring antiviral substance that inhibits the growth of many different viruses; these are, of course, resistant to the known antibiotics. It seems that the cells of birds, rodents, and many mammals, including man, respond to infection by any of a variety of different viruses by producing interferon.

Interferon was first characterized and studied, as its name may suggest, during an investigation of the phenomenon known as viral interference [1]. Viral interference has been recognized among plant, bacterial, and animal viruses during the past 25 years. Essentially, it is a phenomenon in which cells infected with one virus acquire resistance to super-infection with many other viruses. This general resistance, as opposed to the specific resistance conferred by the antibodies, adds considerably to the interest of the study of interferon. The explanation for viral interference in plant and bacterial viruses is not known, but as far as animal viruses are concerned, many examples of this cellular resistance can be accounted for by the fact that cells respond to virus infection by producing interferon.

When cells are infected with virus and then washed and incubated in fresh medium, they produce an antiviral substance. This has physical and chemical properties that are quite different from those of the virus used to initiate the viral interference. The substance is readily separated from the infecting virus and can then be used to confer some degree of general resistance to viral infection on a fresh population of cells. The resistance produced is essentially a cellular resistance, and interferon, unlike antibody, has no action on extracellular virus. Interferon appears to be of protein or polypeptide nature—its antiviral action can be abolished by treatment with proteolytic enzymes; its physico-chemical properties are consistent with this finding. It has been possible to achieve a certain degree of purification of interferon [12]. When tested by its behaviour on centrifugation and by its rate of diffusion through agar, interferon was estimated to have a molecular weight of 63 000.

Once interferon is formed within cells, it is rapidly liberated into the surrounding medium so that it has an opportunity to protect some of the neighbours of cells initially infected. This suggested that interferon might play a part in the resistance of cells to viral infection in general, and in the ability to recover from virus infections in particular. In addition, the question can now be posed as to what role interferon might play in the metabolism of the normal cell.

Recovery from viral infection

The process of recovery from viral infection can be studied in cells grown *in vitro*. Since the work of F. B. Bang and G. O. Gey [2], a number of examples have been demonstrated of cells chronically infected with virus *in vitro*. In chronic infections of this kind a virus that under some circumstances might destroy a cell population comes instead to live in relative harmony with the cells. The result is a mild infection that may persist for many months. One possible explanation of the survival of the cells is that, as a result of infection, the cells that are naturally resistant to the virus are selectively favoured. However, it can be shown that this is not the actual reason, as, when chronic infections were cured by one means or another, the cells were found to be susceptible once more to infection by the same virus.

The production of interferon is a very general response by the cells of vertebrates to virus infection, and it is natural, therefore, to wonder whether chronic virus infections could be explained by the production of interferon. It has in fact been found by a number of workers that interferon accumulates in chronic virus infections of cells *in vitro*. Recently, L. A. Glasgow and K. Habel [3] have provided a convincing demonstration that interferon plays an important role in determining the course of chronic infections. These workers showed that in mouse cells chronically infected with vaccinia virus, repeated changing of the culture medium, or treatment with small amounts of trypsin, kept the concentration of interferon low and resulted in destruction of the cells by virus. Conversely, if the medium was changed infrequently and some old medium left behind, the concentration of interferon remained high, and this led to complete cure of the virus infection. A middle experimental course gave rise to a persistent virus infection that could be maintained for many months (figure 1). One chronic virus infection that occurs in man is herpes simplex, which may show itself as an eruption of vesicles around the mouth in fevers. These experiments suggested that the course of such chronic virus infections *in vivo* might be influenced by the amount of interferon produced locally.

It is more difficult to evaluate the role of interferon in recovery from viral infections *in vivo* than in the case of infections *in vitro*, as recovery is a complex process, involving, for example, the production of antibodies. The chick embryo is the least complicated of the animals studied; its ability to recover from many virus infections cannot be ascribed to production of antibody or to development of delayed hypersensitivity, as these are known not to occur in the chick embryo. Resistance of the chick embryo to viral infections has been shown [4] to be related in time to the development of the interferon mechanism—both develop at the same rate. Thus interferon production and sensitivity to the antiviral action of interferon were both found to be poorly developed in chick embryos less than 7 days old. After that time the embryos matured as regards both the ability to produce good yields of interferon and the development of sensitivity to its antiviral action. At the same

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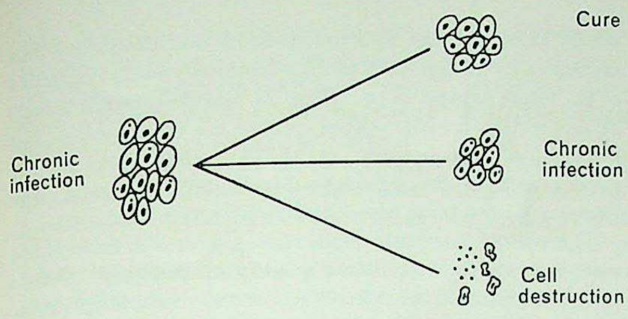

Figure 1 *Diagram illustrating the possibility of affecting a chronic viral infection in one of three different directions by alteration of cultural conditions.*

time the embryos acquired resistance to lethal infection with a number of different viruses. This is presumptive evidence that in the chick embryo, as in cultures infected *in vitro*, interferon plays a role in recovery from virus infection.

The mature vertebrate responds to virus infection by producing interferon at the site of virus multiplication during the early stages of the infection. Later, the animal produces specific antiviral antibody, and this leads to prolonged resistance to re-infection by the same virus. In some virus infections, delayed hypersensitivity may also develop. It is, however, difficult to evaluate the respective contributions of these three factors, and of many other factors, such as fever, to the process of recovery from virus infection. It seems, nevertheless, that the production of antibody may play a less significant role in recovery than was formerly believed.

Virus virulence

Viral genetic studies show that the virulence of viruses, that is their lethal effect on cells, is a complex and multigenic property. Very little is known of the factors on which virus virulence depends, so that interest was aroused by the observation of J. F. Enders [5] that an avirulent measles virus induced a higher production of interferon than a virulent one; the same seems to be true of a number of polioviruses. Enders speculated that these observations might be relevant to the general problem of virus virulence.

Recently, there have been a number of investigations that tend, on the whole, to support this generalization. In addition, it has been found that virulent viruses are usually less sensitive to the antiviral action of interferon than avirulent viruses [6]. Virus mutants that differ in virulence for a particular animal host, or for certain animal cells *in vitro*, have been found to show distinct differences in both the production of interferon and in sensitivity to the antiviral action of interferon. Virulent mutants were found to stimulate cells to make less interferon than avirulent mutants. The virulent mutants were also found to be less sensitive to the antiviral action of interferon than the avirulent mutants. All of these findings suggest that a significant factor in viral virulence may be the ability of a virus to evade a normal defensive response of cells to virus infection.

Virus virulence and interferon production share one characteristic in common. They are not isolated properties of a virus, but describe the behaviour of a virus in relation to a particular population of cells. This is shown very convincingly by the virus that causes fowl pest (Newcastle disease virus). It is very virulent for adult chickens and chick embryos, it grows well in chick embryo cells *in vitro*, and it produces poor yields of interferon. The same virus shows low virulence for man, grows poorly in human cells *in vitro*, but it induces the production of large amounts of interferon.

Cellular and viral nucleic acids

A virus is nowadays seen as nucleic acid, wrapped in a tightly fitting protein overcoat and ready to deliver its 'instructions' to the cell to synthesize more virus. Earlier, the syntheses of virus nucleic acid and of normal cellular nucleic acids were sometimes described as overlapping processes. They were, that is, considered to be processes so similar that it would be impossible to affect one without affecting the other. It would, if this were so, be impossible to prevent virus replication without affecting the normal replication of cells. However, there has recently been evidence from the study of animal viruses of the independence of the two processes. Treatment of cells with actinomycin D has been shown to inhibit the synthesis of normal cellular RNA without inhibiting the replication of certain RNA viruses. Similarly, treatment of cells with mitomycin has recently been found to inhibit the synthesis of normal cellular DNA without inhibiting the replication of the DNA-containing adenovirus. The independence of the two processes encourages the idea that it should be possible to inhibit the synthesis of viral nucleic acid without inhibiting the synthesis of normal cellular nucleic acids, and some evidence that this can occur in cells treated with interferon will later be mentioned.

The first reaction to the initiation of virus infection is that cells manufacture enzymes required for the synthesis of viral nucleic acid. Under the influence of viral RNA polymerase, which is probably different from the normal cellular RNA polymerase, nucleotides are joined together to form viral RNA. Later, the protein of the viral coat is synthesized and then becomes fused with the nucleic acid to form mature virus particles, which are then liberated from the cell. In some infections, virus multiplication leads to complete disorganization of the cell. But with most virus infections there is an element of orderliness about the multiplication process. The synthesis of viral nucleic acid and protein does not continue indefinitely; it usually halts and allows the cell to recover from the infection. This implies that there are regulators of the process of virus multiplication in animal cells, analogous to the regulators demonstrated by Jacob and Monod in connection with bacteriophage infection of *E. coli* and with the processes of enzyme induction. It seems likely that interferon is a regulator of this kind in animal cells.

It has been found that when cells are treated with amounts of interferon that greatly inhibit virus growth, the rate of cell division is not significantly inhibited [7, 8]. However, when very large doses of interferon were used, for example 2000 times the minimal dose required to produce 50 per cent inhibition of virus growth, the rate of growth of the cells was slowed, and gradually returned to its normal rate when the interferon was removed [8]. Clearly the synthesis of viral nucleic acids or proteins is much more readily inhibited by interferon than is the synthesis of normal cellular nucleic acids and proteins.

Interferon does not inhibit adsorption of virus by cells or its penetration of the cells. What it does is to block viral multiplication at a stage after the viral nucleic acid and protein have become separated, but before the viral nucleic acid has been replicated [9]. We have no knowledge at present of the mechanism by which the synthesis of viral nucleic acid is prevented.

The stimulus to make interferon

Interferon was first detected in cells treated with inactivated virus [1], and many experiments show that virus multiplication is not necessary in order to stimulate cells to produce interferon. This implies that the essential stimulus that does induce cells to make interferon is a viral constituent brought by the

Table I

Antiviral action of chick and mouse RNA on vaccinia virus grown in chick and mouse cells

Material tested	Concentration	Mean virus plaque count in mouse cells	Mean virus plaque count in chick cells
Control	—	19	175
Chick RNA	50γ/ml	5	126
	10γ/ml	11	182
Mouse RNA	50γ/ml	11	0
	10γ/ml	14	29

virus particle to the cell. Viral protein and viral nucleic acid were the main suspects, and indirect evidence tended to incriminate viral nucleic acid.

These results raised the question as to whether there is something particular about viral nucleic acid or whether non-viral nucleic acids could have a similar action. This is a technically difficult problem, since non-viral nucleic acids are poorly taken up by cells. However, some recent experiments in our laboratory [10] show that production of interferon, although only in relatively small amounts, can occur as a result of stimulation with non-viral nucleic acids. These experiments were prompted by the hypothesis that production of interferon was the response of the cell to a foreign nucleic acid, the word 'foreign' being used to describe the fact that numerous RNA and DNA viruses, both live and inactivated, are capable of initiating the production of interferon in a single population of cells.

In order to test this hypothesis, RNA was prepared from microsomes of the livers of chicks and mice. The RNA preparations were then tested for their antiviral action in chick cells and in mouse cells. If RNA were inducing cells to make small amounts of interferon, this would be shown by the ability of the RNA to protect cells against virus infection. What was found was that 'foreign' RNA was effective; chick RNA protected mouse cells and mouse RNA protected chick cells (see table). Protection by homologous RNA was always less than protection by foreign RNA and was frequently not demonstrable at all. Small degrees of protection by homologous RNA could be due to the fact that inbred animals were not used, so that small differences between the RNA preparations and the nucleic acid of the homologous cells probably exist. This question is now being investigated with inbred animals.

The role of interferon in normal cells is not known, and until recently there was little reason to suspect that it might have some function apart from its effect on viral multiplication. Recently, however, my colleague E. Heller [11], while investigating the effect of actinomycin D on virus multiplication, observed that the production of interferon was strongly inhibited. Actinomycin is known to inhibit the synthesis of RNA that is under the control of cellular DNA. As a result, it does not inhibit the growth of certain RNA viruses that are not dependent on cellular DNA. However, the fact that it inhibits the production of interferon implies that interferon synthesis is under the control of cellular DNA. This suggests that interferon has a role to play in the economy of the normal cell, presumably connected with the synthesis of certain cellular nucleic acids. Unfortunately, it is not possible to be more precise than this at the moment, but the nature of this action should be a fascinating topic for future research.

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Book reviews

MATHEMATICAL TABLES

An Index of Mathematical Tables ***(second edition), by A. Fletcher, J. C. P. Miller, L. Rosenhead, and L. J. Comrie. Vol. I, pp. xi+608; Vol. II, pp. iv+609–994. Published for Scientific Computing Service Ltd, by Blackwell Scientific Publications Ltd, Oxford. 1962. £15 net.***

It is a tribute to the authors of this work that this second edition has been so anxiously awaited; now that it has come, it more than fulfils our expectations. The major part of the work is the 600-page 'Index According to Functions' which, with an introduction, constitutes Volume I. Volume II contains a bibliography, listed according to authors, of works referred to in Volume I; a section on known errors in published tables; and an index. The latter now includes authors as well as functions, and is much more valuable to the reader than that of the first edition.

It takes a long time to see a work like this through the press, so that the authors are to be congratulated on having kept it so up to date. There are numerous references to tables published in 1960, and some to 1961. Moreover, the authors' extensive knowledge of computing activities has enabled them to include many references to tables which have yet to be published. The section on errors was largely compiled by the late L. J. Comrie and makes fascinating reading.

No laboratory in which any computing is done can afford to be without this Index, for which the computing world owes the authors a deep debt of gratitude.

E. T. Goodwin

HIGH-PRESSURE TECHNIQUES

Modern Very High Pressure Techniques, ***edited by R. H. Wentorf, Jr. Pp. xiv+233. Butterworths, London. 1962. 60s. net.***

This book is a useful addition to the literature of research on high pressures, since it provides for the first time a wealth of information on basic techniques in the ultra-high pressure range. In this respect it is a welcome change from publications recording the proceedings of scientific meetings. The book may be used as a supplement to Bridgman's published work, and it contains some new material, including the details, given by B. von Platen in perhaps rather too flowery a style, of the remarkable Swedish cubic press for diamond synthesis, and the description of experimental techniques given by another industrialist, L. Coes. The production and measurement of very high pressures over a range of temperature are described, together with some application to phase change and geochemistry (H. M. Strong, L. Coes, F. R. Boyd, R. Roy, and F. Dachille). Because of the range of pressure chosen, most authors limit their remarks to the solid state, or to phase changes involving solids. Two of the most urgent problems in this field, the calibration and the extension of the pressure range, are excellently treated by F. P. Bundy, and by H. G. Drickamer and A. S. Balchan. The upper static pressure limit of about 500 000 atm can be extended by a factor of about ten by the use of shock waves, as described by W. E. Deal. Readers of this book will realize that the cost of high-pressure equipment has risen far beyond the cost of that used in the pioneer work of Bridgman and that it is difficult for universities to compete with industrial laboratories. The chapters by C. E. Weir, A. van Valkenburg, and E. Lippincott, and by J. C. Jamieson and A. W. Lawson, on optical studies and on X-ray studies, show, for example, how useful good-quality diamonds are in this work.

It is clear from this book that a new engineering science is developing, and indeed much of the equipment is now commercially available. This book can be strongly recommended both to workers in the field and to interested onlookers. *R. S. Bradley*

THERMODYNAMICS

Entropy, *by J. D. Fast. Pp. xii+313. Philips Technical Library; Cleaver-Hume Press Ltd, London. 1962. 57s. 6d. net.*

This excellent book by the chief metallurgist of Philips' Research Laboratories should be welcomed by physicists and chemists alike. It is clear, concise, and well thought out, and could be read with profit by both research workers and students. For the latter it would be a good introduction to both statistical thermodynamics and the applications of thermodynamics in solid-state physics and chemistry.

The chapters on the statistical meaning of entropy are particularly clear. They introduce the important physical ideas first, by means of well chosen examples, and avoid in an exemplary fashion the use of unnecessarily elaborate mathematics. A particularly stimulating feature of the book is the way that free energy is used as a physical concept rather than as a mathematical device, so that the significance of both the terms U and $-TS$ in determining the equilibrium of a system becomes apparent.

Apart from the expected topics, the applications of the concept of entropy include some more unusual ones, such as to heat pumps and to the thermodynamics of polymer solutions. The treatment of these adds to the up to date flavour of the book and also underlines the importance of entropy.

The translation by Mrs Mulder-Woolcock is both clear and readable.

F. N. H. Robinson

ELECTRON MICROSCOPY

Electron Microscopy, a Textbook for Students of Medicine and Biology, *by Gilbert Causey. Pp. vii+238. E. & S. Livingstone Ltd, Edinburgh and London. 1962. 48s. net.*

Morphology received a fresh impetus with the advent of the electron microscope, and the importance of ultra-structural concepts is already such that they must find some place in undergraduate instruction. To convey a coherent pattern of a rapidly expanding field is not easy, but Professor Causey has now essayed this important task with success.

His account is confined to normal ultrastructure. After referring briefly to techniques and the validity of electron-micrographic appearances, he describes the basic components of cells in general and then discusses the systems of the body in turn. The coverage appears somewhat uneven, but this merely reflects the current state of knowledge. Variations in the distribution and preponderance of subcellular elements in different cells are stressed in an attempt to elaborate functional concepts. The sections on the alimentary and renal tracts particularly show how this correlation of structure and function may be achieved.

A growing subject poses many questions. Professor Causey makes clear that further advances may be expected by a study of ultrastructure firstly in different functional states, and secondly after experimental treatments.

Illustrations are numerous, although some electron micrographs could be improved. Students, who will derive much benefit from this valuable book, might welcome more diagrams. *A. G. Heppleston*

CHEMICAL DICTIONARY

Dictionary of Chemistry and Chemical Technology in Four Languages, English/German/Polish/Russian, *edited by Z. Sobecka, W. Biernacki, D. Kryt, and T. Zadrozna. Pp. 724. Pergamon Press, Oxford; Wydawnictwa Naukowo-Techniczne, Warsaw. 1962. £10 net.*

The card index of chemical terms in the Polish Technical Publishing Institute contains 105 000 entries that were used as the basis of selection of the very much smaller number of terms in the present compilation —totalling 12 000 after the addition of entries from more recent literature. A four-language dictionary containing even this relatively modest number of terms is a great consumer of paper, especially when, as here, exhaustive cross-indexes in the different languages are provided with the praiseworthy objective of making the work equally useful to readers whose native languages are English, German, Polish, or Russian. And so we have 724 pages of large format as the fruit of the labours of several editors faced with the unenviable task of catering, in a volume of reasonable size, for the linguistic needs of a heterogeneous collection of readers of chemical literature. Some degree of success has admittedly been achieved in the field of what may be called basic chemical science and practice. This cannot be said, however, of the various branches of chemical technology; nor could it be expected.

Having made the point about the limitations of the content of the dictionary, it is only fair to add that it fills a gap in respect of its multilingual coverage, that it is beautifully printed; and that the layout is superb. Altogether, it is a sumptuous production that can be highly commended to chemical libraries. *L. Light*

VALENCY THEORY

Hyperconjugation, *by Michael J. S. Dewar. Pp. vi+184. The Ronald Press Co., New York. 1962. $6.*

The appearance of the new book by Professor Dewar is a scientific event. Like his first book, this one is a challenge to orthodoxy. The author's great breadth of knowledge and theoretical understanding have enabled him to survey critically the theoretical basis and the experimental evidence for the much debated concept of hyperconjugation. He argues, on the whole convincingly, that most evidence for hyperconjugation is capable of interpretation without the use of this concept, and he traces much of the current confusion to the misconception that valence electrons may be more or less localized in different bonds. When Professor Dewar has finished with the concept, there seems to be very little left of it, at least as an aid to describing the ground states of molecules. He concedes that it occurs in free radicals, carbonium ions, and the excited states of molecules, but recommends its dismissal from discussions of ground-state properties.

The book is well written, closely argued, and eminently stimulating. It is likely to arouse disagreement and certain to lead to further research. *H. C. Longuet-Higgins*

ANALYTICAL CHEMISTRY

Treatise on Analytical Chemistry, *edited by I. M. Kolthoff and P. J. Elving, with the assistance of E. B. Sandell. Part II,* The Analytical Chemistry of the Elements. *Vol. 2,* Gallium, Indium, Thallium, Silicon, Germanium, Iron, Cobalt, and Nickel. *Pp. xx+471. £6 15s. net; Vol. 7,* Sulphur, Selenium, Tellurium, Halogens, Manganese, Rhenium. *Pp. xxiii+567, £6 19s. net; Vol. 9,* Uranium and the Trans-uranium Actinides. *Pp. xvi+491, £6 15s. net. Interscience Publishers, a Division of John Wiley & Sons, New York and London. 1962.*

For each element in these volumes, there are notes on occurrence, uses, toxicology, and chemical and physical properties (including, for some elements, standard electrode potentials and stability constants of selected complexes). Then follow sections on methods of separation, detection, and chemical determination, and, where appropriate, notes on spectrography. Finally, there are sections on 'specific' methods or 'determination in specific materials'. The analysis of commercial materials will constitute Volume 3. The literature has been reviewed to 1957 or 1958, with a few references to 1959. The reviewer notes that a few papers have been missed, but even so there are, for example, almost four hundred references to iron.

Naturally, as each monograph is by a different author, the treatment is uneven. The reviewer would like to commend in particular the monograph on sulphur (inorganic compounds only), though the thionic acids are but cursorily treated, and that on silicon; but obviously these volumes will be most useful to the experienced analyst where they deal with unfamiliar elements such as rhenium. No reviewer not engaged in the atomic-energy industry can comment on the amazing mass of information in Volume 9 on the actinides, especially the trans-uranium elements; one can but respectfully admire the learning and manipulative skill expended on this subject in the last twenty years. *H. N. Wilson*

GAS CHROMATOGRAPHY

Biochemical Applications of Gas Chromatography, *by H. P. Burchfield and Eleanor E. Storrs. Pp. xviii+680. Academic Press, New York and London. 1962. £7 17s. net.*

In the ten years since its inception, gas chromatography has become an indispensable analytical tool in many branches of pure and applied biochemistry. It was the authors' intention to supply a textbook covering the theoretical background and the principles of the various techniques, and also to give such details of laboratory procedures as are necessary for a laboratory manual. In over 300 cases, the authors sent the draft manuscript to the originators of procedures for comment, and incorporated their improvements and additions. On these practical aspects, the book offers rather more than other textbooks in this field. Ancillary methods such as sample collection, prefractionation of the samples by liquid-solid chromatographic and ion-exchange techniques are covered. So, too, are procedures for the preparation of stationary liquids and chromatographic columns, removal of unwanted compounds from the gas stream, and the synthesis of derivatives of non-volatile compounds that are themselves amenable to gas chromatography. In view of the ever-growing importance of the technique, this competent and up to date textbook will be welcomed by many biochemists. *H. A. Krebs*

INORGANIC CHEMISTRY

Advanced Inorganic Chemistry: A Comprehensive Text, *by F. A. Cotton and G. Wilkinson. Pp. xv+959. Interscience Publishers, a Division of John Wiley & Sons, New York and London. 1962. £5 5s. net.*

Inorganic chemistry has developed with astonishing rapidity during the last twenty years. Not only have important types of compound been discovered, but underlying theoretical principles have been formulated and extensively applied. The authors of this book have been outstandingly successful in giving a comprehensive account of the descriptive chemistry of the elements against a background of modern theory. The treatment is at a level which is suitable for the final year of an honours degree course. The non-transitional elements are dealt with in a series of chapters, the most notable features of which are the emphasis on structural chemistry and the complete absence of the 'catalogue' approach, which has done so much to kill interest in inorganic chemistry in the past. Some of the sections, such as that on boron hydrides, are particularly good, and well-chosen references to monographs and review articles should serve as a guide to topics that are less fully covered.

The section on the transition elements is prefaced by chapters on their general properties. These cover a number of subjects that figure prominently in current research. The remaining descriptive chemistry is dealt with by reviewing the transition series. In the writer's opinion, these chapters are rather overburdened with detail in comparison with the earlier chapters on the non-transitional elements, though the authors' treatment could be justified by the generally rather inadequate discussion of these elements in other texts. The book is one that can be recommended without any reservations both to undergraduates and to research workers. It is the best advanced textbook of inorganic chemistry that has so far appeared, and it can hardly fail to stimulate interest in the subject and modernize its teaching.

H. J. Emeléus

ORGANOPHOSPHORUS COMPOUNDS

Organophosphorus Monomers and Polymers, *by Ya. L. Gefter (translated from the Russian by J. Burdon). Pp. vii+302. Pergamon Press Ltd, Oxford. 1962. 70s. net.*

This book develops especially the part of organophosphorus chemistry that is relevant to high polymers; its aim is to systematize the existing knowledge of the basic properties of phosphorus-bearing monomers and polymers. In the first part, the chemistry of the monomers is described in two chapters—one on the preparation of compounds in which unsaturated groups are attached to phosphorus, the other on compounds containing bifunctional groups involving phosphorus. Practical details are given for the synthesis of many key compounds, and the physical properties of many more are tabulated. Most of the information in the book is presented in this way; tables occupy more than half the book. The second part follows the same pattern, and deals successively with polymers that contain phosphorus in side groups and in the polymer chain, but it is less satisfactory. Few of the 'monomers' form good polymers, and only the broadest information is available on polymer properties. The benefits conferred by phosphorus, such as reduced flammability, appear incidental, and the last section, on applications, does not grow naturally out of the earlier chapters. The value of the book is mainly in its tables, which collect a vast amount of information in a convenient form.

N. L. Paddock

METAL COMPLEXES

Absorption Spectra and Chemical Bonding in Complexes, *by C. K. Jørgensen. Pp. xii+352. Pergamon Press, Oxford. 1962. 70s. net.*

The purpose of this book is to summarize recent work on the electronic spectra of metal complexes and particularly to show the importance of these developments for the theory of chemical binding.

The book begins with an account of atomic and molecular orbitals and of the energy levels associated with them. These first six chapters contain much valuable information, but a newcomer to the subject would find them very difficult and not very illuminating. The following chapters are on the spectrochemical series, the nephelauxetic series, and on electron-transfer spectra. These are very interesting accounts of work done, and the summaries of all the data will be of great value to inorganic chemists. The use of the molecular-orbital theory for the description of the energy levels of various types of complexes is described. The advantages of the molecular-orbital method over the valence-bond method for the discussion of spectra are emphasized particularly in chapter 12. The problems of studying spectra in solutions where complex equilibria exist are considered in chapter 13.

The rest of the book is a summary of the spectra of all types of inorganic complexes and includes valuable tables and references. The book contains much material of great interest, though it is a pity that the subject matter is presented in such a heavy and indigestible form. *R. E. Richards*

RADIATION CHEMISTRY

Radiation Chemistry of Polymeric Systems, *by A. Chapiro. Vol. XV.,* **High Polymers.** *Pp. xvi+712. Interscience Publishers, a Division of John Wiley & Sons, New York and London. 1962. £7 18s. net.*

This book is an extensive treatise on the radiation chemistry of polymers and polymerizable systems, and will be of particular interest to those concerned with the nature of the chemical reactions. Apart from rubber and cellulose, naturally occurring polymers are not dealt with.

Initial chapters on radiation physics, primary radiochemical processes, and the radiation chemistry of lower hydrocarbons, are followed by the main part of the book dealing with the effect of high-energy radiation on polymers and their solutions, on polymerization initiated by radiation and on graft copolymerization techniques. Although all these topics are treated in great detail, with very extensive reference to the literature, the book is planned so that the more general chapters provide a good introduction to the radiation chemistry of organic systems, with particular emphasis on the high polymers. The more detailed chapters will be invaluable to the specialist.

Dr Chapiro has produced a critical account of present knowledge of his subject, and has written a book that will be of considerable value for some time to come.

P. P. Manning

ORGANIC CHEMISTRY

Principles of Organic Chemistry *(second edition), by T. A. Geissman. Pp. x+854. W. H. Freeman & Co., San Francisco and London, 1962. 35s. net.*

The appearance of the amplified second edition of this textbook shows that the mechanistic approach to organic chemistry now has the support of very many university teachers. In Britain, there is a need for moderately priced volumes to fill the gap between school textbooks and the comprehensive treatises on organic chemistry that so often present first and second year honour students with indigestible masses of facts or sophisticated accounts of theories. To these students, this book can be commended for its readability.

Geissman names the main functional groups of organic compounds and then explains why they react as they do, instead of listing for memorization how various types of organic compounds can be prepared and stating their reactions. By starting with pictorial diagrams of bond orbitals and with mechanistic stereochemistry, resonance theory and the main features of aliphatic and aromatic chemistry are successfully presented as one coherent subject, clarified further by the use of simplified presentations of bond polarization and electromeric change. In later chapters this treatment is gradually abandoned, as additional reactions and many complex compounds are categorically described on grounds of special interest. Heterocyclic chemistry receives very inadequate mention. In the closing chapters the biological importance of organic compounds becomes the main theme.

W. A. Waters

FLAVONOID CHEMISTRY

The Chemistry of Flavonoid Compounds, ***edited by T. A. Geissman. Pp. vii+666. Pergamon Press, Oxford. 1962. £7 10s. net.***

The wide distribution of the flavonoids in plants, to many of which they contribute characteristic features of colour and taste, has been responsible for innumerable investigations into their chemistry. The publication of a monograph comprehensively summarizing the accumulated knowledge of this varied group of plant phenols for the first time is thus a notable venture.

The first six chapters give general accounts of the occurrence of flavonoids; their extraction, separation, and identification; their characterization by means of spectra; and their interconversion by controlled oxidation and reduction. Special features of their chemistry, including synthesis, are discussed in the following seven articles on catechins and flavonoid tannins; leucoanthocyanins and leucoanthocyanidins; anthocyanins; flavones, chalcones, and aurones; glycosides of flavones and flavonols; isoflavones and flavones. The remaining sections deal with their stereochemistry and their economic importance, and with chemico-genetical studies and biosynthesis.

Full literature references are given in each chapter and the book is well furnished with structural formulae, diagrams, and tables of physical properties and other data. Except that two or three chapters are too largely catalogues of detail, the various articles are well balanced; and although each is self-contained there is no unnecessary duplication of material. Authors, editor, and publishers have done their work well and have produced an attractive and authoritative treatise.

F. E. King

CRYSTALLOGRAPHY

International Tables for X-ray Crystallography, ***General Editor: Kathleen Lonsdale. Vol. III,*** **Physical and Chemical Tables,** ***edited by Caroline H. MacGillavry and Gerard D. Rieck. Pp. xvi+362. Published for the International Union of Crystallography by The Kynoch Press, Birmingham. 1962. £5. 15s. net.***

It is a happy coincidence that the final volume of International Tables for X-ray Crystallography has appeared at a time when attention has been directed to the subject by the award of two Nobel Prizes. In this volume the physical and chemical data required by crystallographers have been collected either from the literature or from measurements made specially for inclusion in the tables.

So many subjects are covered, including, for example, refractive indices of liquids, the wavelengths of X-rays, and interatomic distances, that it is impossible to attempt to enumerate them in a short review. It can fairly be said that the index of Volume III, which also covers Volumes I and II, is the first place for a crystallographer to look for information, and it is difficult to think of any subject that has not been covered.

The tables themselves are well laid out, and there is a lucid and critical explanation for each one. Many authors have contributed to this volume, and all X-ray crystallographers will be most grateful to them, to the editors, and to the publishers for such an excellent book.

M. R. Truter

Fifty Years of X-ray Diffraction, ***edited by P. P. Ewald. Pp. ix+720. Published for the International Union of Crystallography by N. V. A. Oosthoek's Uitgeversmaatschappij, Utrecht. 1962. 80s. net.***

Whatever scientific advances are made in the second half of the twentieth century, the great achievements of the first half will not be overshadowed. Among these the discovery and development of X-ray diffraction stands out as an extremely impressive story with far-reaching and important consequences for science and technology. Our present knowledge of solid-state physics, chemistry, and biology owes much to the development of the techniques of X-ray crystal structure analysis, and our knowledge and control of the atom grew from the insight provided by X-ray spectroscopy.

In July 1962, the fiftieth anniversary of von Laue's discovery of X-ray diffraction was celebrated in Munich by a large international gathering of scientists. This book was published to mark the occasion and is dedicated to the International Union of Crystallography. It traces the progress in the science and application of X-ray techniques from their beginnings to the present day and it does so in a very lively way through the pens of those who themselves laid the foundations of the subject.

The major part is devoted to a review of the original discovery, and of the development of crystal structure analysis, of spectroscopy, and of crystal optics. Among the contributors to this section are W. L. Bragg, Hume-Rothery, Wyckoff, Kathleen Lonsdale, Ewald, and Siegbahn. The later part of the book strikes a more personal note with interesting biographies and reminiscences from a host of famous names and places.

R. L. Bell

OCEANOGRAPHY

Introduction to Physical Oceanography, ***by W. S. von Arx. Pp. x+422. Addison-Wesley Publishing Co. Inc., Reading, Mass. and London. 1962. £5 13s. net.***

This book gives a comprehensive and concise account of the aims and achievements of the subject and answers the searching questions that enquiring students are likely to ask. The generous approach to the subject also directs attention to many things that research workers, especially those in related fields, will find useful. The author deals with the history and geology of the oceans, with the characteristics of sea-water and with the theoretical, experimental, and observational study of the forces and movements. Difficult concepts in the theory of tides, waves, and currents are presented in a remarkably clear and attractive way. He gives a clear account of what we know of the interchange of energy between ocean and atmosphere, the generation and propagation of waves, surface currents, deep-water circulation, and the processes that are still shaping the ocean floor. Special chapters are devoted to the author's own main interests —current measurements by direct and indirect methods, laboratory models, and the Gulf Stream problem. Appendix A contains a very useful and well-chosen list of stages in the development of the subject, and the other appendices give useful constants and tables. The book can be thoroughly recommended to teachers, and to students approaching degree standard, as well as to anyone concerned with the science of the sea. Frequent references to the historical development of the subject add much to the charm of the book.

G. E. R. Deacon

THE MECHANISM OF MEMORY

Macromolecular Specificity and Biological Memory, ***edited by F. O. Schmitt. Pp. 119. The M.I.T. Press, Massachusetts Institute of Technology, Cambridge, Mass. 1962. $3.***

There can be few serious scientific publications that contain such orgies of speculation as this one. Its 119 pages contain 25 articles, many by distinguished authors. There is no attempt to disguise the speculation. As the editor admits, no investigations are even under way concerning the 'physical or chemical processes specific with respect to the primary monomer sequences that provide the readout of the coded information in the nervous system'. This is simply to say that we have not even thought of a means of testing whether molecular sequences have anything to do with the neural memory.

Nevertheless, these short abstracts are absorbing and often exciting. Such very exact investigations as those of Hydén by which the base sequences of the RNA in single neurons are analysed and found to change with excitation must advance the subject.

It would be interesting to hold a similar symposium devoted only to criticism by each author, either of himself or of others.

J. Z. Young

MUCOPOLYSACCHARIDES

Biochemistry and Medicine of Mucopolysaccharides, *edited by F. Egami and Y. Oshima. Pp. 321. Research Association of Mucopolysaccharides, University of Tokyo; Maruzen & Co. Ltd, Tokyo. 1962. £4 14s. 3d. net.*

For many years Japanese scientists have been active in research on mucopolysaccharides and mucoproteins—those complex combinations of nitrogen-containing sugars, hexoses, and amino acids that are present as macromolecules in all animal tissues.

A few years ago a research group was set up in Japan under the chairmanship of the distinguished chemist, the late Professor H. Masamune, to investigate various aspects of mucopolysaccharide chemistry and biochemistry. This book describes the results of the first three years work of the group and it consists essentially of 24 interim reports by some 60 authors on a wide range of topics in the field.

Apart from two articles that are essentially reviews on the chemistry and biochemistry of these substances, the chapters are highly specialized. As such, they will be of the greatest interest to other workers in the field who will be able to distinguish the new material from the old. There is indeed a lot of fresh material described, especially on the biological side. New chemical work is mainly concerned with isolation and fractionation techniques with considerable analytical data and some physical measurements. No new structures are provided. Some new names used for compounds only add to confusion of nomenclature in this field. Many of the reported results and the speculations are interesting but they will doubtless have to stand up to severe criticism later. The standard and style of English is only just adequate and there are a number of misspellings and misprints. The tables and plates are good and the printing is quite good. Many chapters fail to carry a summary, and in most chapters, 60 per cent or more of the references are to Japanese work. The book will be of great interest to specialist workers in a field that is undoubtedly of growing importance in medicine and biology generally. One cannot but be impressed by the magnitude of effort which the Japanese scientists are putting into this field of investigation, and the book will act as a stimulus to other workers in laboratories all over the world.

M. Stacey

PROTEIN CHEMISTRY

Polyamino Acids, Polypeptides and Proteins, *edited by Mark A. Stahmann. Pp. xviii + 394. The University of Wisconsin Press, Madison. 1962. $8.*

This volume will be of equal interest to scientists primarily concerned with the chemistry of polymers in general and to workers who consider polyamino acids mainly as useful models for naturally occurring peptides and proteins.

The first part of the book gives a review of synthetic methods and of problems of conformation, which are considered in several articles. Hofmann and Yajima give an interesting account of preparative problems, particularly those concerned specifically with arginine, and Kovacs discusses aspects of the chemistry of glutamic and aspartic acid and their polymers, with particular emphasis on the contributions made by Hungarian workers.

The next two parts are devoted to a consideration of the mechanism of the polymerization reaction and also to the properties of the polyamino acids in solution. They show clearly that the study of polyamino acids has led to a better understanding of the relationship between helical conformation and optical rotation. Other optical studies, such as those of Elliott and Doty, and of Scheraga are also noteworthy.

On the more biological side, this volume contains an interesting account by E. Katchalski on the use of water-insoluble derivatives of proteolytic enzymes. Another interesting development to which this group and Paul Doty and his colleagues have made important contributions is concerned with immunology. It has been shown, for example that, while tyrosine plays an important part in conferring both immunological activity and specificity on a polypeptide, some polymers not containing this aromatic amino acid are good antigens.

The volume is well produced, free from typographical errors, and is altogether a useful account of this important field of chemical research.

A. Neuberger

BIOCHEMISTRY

Horizons in Biochemistry, Albert Szent-Györgyi Dedicatory Volume, *edited by Michael Kasha and Bernard Pullman. Pp. xiv + 604. Academic Press, New York and London. 1962. £5 14. 6d. net.*

Szent-Györgyi's personal horizons were certainly wide-ranging, as Wurmser shows in the opening chapter. This also indicates the reason for the structure of this book. The theme of biochemical evolution is developed through molecular genetics, biochemical catalysis, molecular organization, biochemical molecular structure, and quantum biochemistry by over 30 distinguished scientists. Space almost precludes comment, but Melvin Calvin's consideration of the role of photosynthesis in the evolutionary process pleased me greatly. There are three contributors from Britain: H. A. Krebs makes a timely physiological point neatly and with experimental detail in a short space; D. D. Eley writes on a subject upon which I know I have no competence to comment; and whilst I have tremendous admiration for J. D. Bernal's contribution within his own scientific speciality, I find him less penetrating in his present speculations. It is surely strange to learn that the underlying unity in biochemistry that implies a biochemical evolution was the main new idea of the fifth Biochemical Congress in Moscow; it has been a constant theme in biochemical teaching for some 25 years.

George Wald in his 'Why Phosphorus and Sulphur for High-energy Bonds?' reflects the irrepressible humour of Szent-Györgyi who, at international congresses and elsewhere would charm us with his vision as well as his puckish wit. The unity which these writers have achieved in this book is remarkable and the editors can be congratulated; it is generally readable, often stimulating, and always informative.

Frank C. Happold

THE EYE

The Eye, *edited by Hugh Davson. Vol. I,* Vegetative Physiology and Biochemistry of the Eye. *Pp. xv + 440. £5 net; Vol. II,* The Visual Process. *Pp. xviii + 796. £7 17s. net; Vol. III,* Muscular Mechanisms. *Pp. xvi + 323. 86s. net; Vol. IV,* Visual Optics and the Optical Space Sense. *Pp. xvii + 432. £5 net. Academic Press, New York and London. 1962.*

The subject of the eye and vision is indeed vast, embracing anatomy and optics at the one extreme, traversing vegetative physiology and biochemistry, and extending into the realms of the psychology of perception at the other extreme. To combine all these many disciplines into an integrated account is an ambitious project, but a considerable success has been attained in these four volumes. The first volume deals with the vegetative physiology and biochemistry of the eye; the second with the visual functions in man, including the physiology of vision, the photobiology of the visual pigments, and the neurophysiology of the retina, the visual pathways, and the visual cortex; the third with the muscular mechanisms involved; and the fourth with visual optics and the space sense. With the exception of Ragnar Granit of Stockholm, the authors are British and American, all of whom have contributed original work to the branch of the subject on which they write. Some sections are better than others: that, for example, on the optical space sense by Kenneth Ogle of the Mayo Clinic and that on neurophysiology by Granit are excellent, as also is the clear exposition of ophthalmic optics. In some sections the views of the author are perhaps stressed too much for the development of the theme to be fully appreciated. The book is too detailed for the junior or casual reader, but on the whole the serious student will find it to be the most readily accessible and comprehensive account available in the English language of the many diverse processes whereby the stimulus of light is converted into perception. Its appeal should be wide, for it will be of great use to all those interested in the eye and vision, whether physiologists, biochemists, or psychologists.

Stewart Duke-Elder

RUMINANT METABOLISM

The Energy Metabolism of Ruminants, *by K. L. Blaxter. Pp. 329. Hutchinson & Co. (Publishers) Ltd, London. 1962. 63s. net.*

Dr Blaxter, by preparing his Clive Behrens lectures in book form, has made his admirable survey of the energy metabolism of ruminants available to a wide audience.

From his knowledge of the methods employed in assessing energy metabolism, he evaluates the apparatus used to study the 'bioenergetics' of ruminants. The expenditure of energy is discussed from the basal level through the various productive processes, together with a consideration of food intake and the specialized digestive and biochemical mechanisms of cattle and sheep.

In the last section, the author makes a critical evaluation of the feeding systems that have found practical application during the last fifty years. Using data that have become available recently, not least from his own laboratory, he suggests that the time has come to devise a system expressing the value of food as metabolizable energy based on kilocalorie units. He then introduces a new method of assessing the value of rations for use in the range of productive situations arising from different physiological states. The author has succeeded in making information accumulated by painstaking effort under laboratory conditions readily available to those concerned with feeding ruminants economically. *F. R. Bell*

AIR POLLUTION

Air Pollution, *edited by Arthur G. Stern. Vol. I, pp. xviii+656. £7 3s. net; Vol. II, pp. xvii+586 £6 12s. net. Academic Press, New York and London. 1962.*

The declared aim of this work is to bring information on the cause, effect, transport, measurement, and control of air pollution to professionals of a wide variety of callings. Such a monumental task necessitates covering many diverse subjects, ranging from atmospheric photochemical reactions to the hydrodynamic capture of airborne dust by sprayed water droplets, and from mathematical models of diffusion processes to air pollution legislation.

Since the editor has confined the work of 52 authors to a total of about 1100 pages, it is to be expected that the specialist will be disappointed by the treatment given to his particular subject. At the same time, however, the editor has been successful in maintaining a high technical level throughout and has avoided the irritating repetition of subject matter common to many multi-authored books.

Volume I covers the nature of air pollution, its deposition, and its effects on plants and animals. It also deals with the sampling and analysis of pollutants. Volume II discusses industrial sources of air pollution, control methods and equipment for air cleaning, and pollution legislation and its administration. Each chapter includes many references to original work. Inevitably, the greatest prominence is given to American research, practice, and legislation, but some mention is made of efforts in other countries; the Clean Air Act passed in Britain merits only three lines in Volume II.

These two volumes should be of most value to the relative newcomer to the field of air pollution, and in view of the widespread awakening of interest in this subject there should be many who will find in them useful information and stimulus. *William Gibb*

THE OVARY

The Ovary, *Vol. II, edited by S. Zuckerman, assisted by A. M. Mandl and P. Eckstein. Pp. xiii+600. Academic Press, New York and London. 1962. £7 17s. net.*

This volume maintains the high standard set by the first volume for concise yet detailed and comprehensive presentation. Most of its fourteen chapters are concerned with the chemistry and metabolism of ovarian hormones and artificial oestrogens, the effects of environmental and experimental agents on ovarian development and function, and the ovarian influence on non-sexual tissues, secondary sex characters, and behaviour. Various authors deal also with the gonads in sex differentiation, with the role of ovarian hormones in the development of the urogenital tract and mammary primordia, with ovarian transplantation, and with the ovary in relation to neoplasia. Clearly the coverage is excellent; indeed, there is a good deal of overlap between chapters, and it is rare to find no, or inadequate, treatment of items that could reasonably be held to lie within the scope of the book.

The few deficiencies found were mostly in peripheral areas of knowledge of the ovary and in those in which the main advances have been made in the last few years, such as the nature of oestrogen inhibitors, properties of oral progestogens, and the means for suppression of ovulation and implantation in the control of fertility. These shortcomings do not influence the overall assessment of the book as one that will most certainly prove invaluable to research workers, clinicians, and academic staff alike. *C. R. Austin*

TECHNOLOGICAL DICTIONARY

Lueger: Lexikon der Technik, *edited by K. Wellinger and E. Krägeloh. Pp. xvi+876. Vol. III, Werkstoffe und Werkstoffprüfung A–Z (4th edition). Deutsche Verlags-Anstalt, Stuttgart. 1961. DM. 180.*

This is the third of a set of three volumes dealing with fundamental principles and forming part of a comprehensive seventeen-volume encyclopaedia of technology. The work has been completely revised and enlarged after an interval of thirty years; the previous edition had only seven volumes. Fifty leading authorities in Germany, Austria, and Switzerland have collaborated in the production of the present volume, which deals with materials and materials testing. The first part of the title covers metals and alloys and non-metals, the latter including such substances as concrete, mortars, plastics, leather, rubber, paper, and bituminous materials. The treatment of materials testing covers chemical and physical principles of testing; tensile, fatigue, and impact testing; high-temperature tests; machinability; weldability; resistance to corrosion, erosion, and cavitation. Non-destructive testing, chemical tests, and metallography are also dealt with. Applications of materials are discussed under the entries for the material themselves, and only occasionally, for example, materials for bearings or nuclear reactor materials, are they entered in their own right. Only a selection of representative tables of physical and engineering data is given, as the encyclopaedia is not intended to replace authoritative volumes of tables. *G. N. J. Beck*

DETONATION AND ROCKET PROPULSION

Detonation and Two-phase Flow, *edited by S. S. Penner and F. A. Williams. Pp. xii+368. Academic Press, New York and London. 1962. 42s. net.*

The volume under review is a collection of research reports, most of which were presented at a conference organized by the American Rocket Society in April 1961. There are six papers on detonations, five on the flow of compressible gas streams containing particles of a different phase, and five on various aspects of rocket-motor combustion.

In the opinion of the reviewer, the interests of the authors and of the readers would have been better served if the papers had been submitted to recognized journals for publication in the usual way. Some of them would then have been rejected on the grounds that the work reported in them was incomplete, and so of insufficient substance. In other cases the editor would have asked the authors to clarify the argument or the meaning of specific sentences. Moreover, those contributions immediately worthy of acceptance would have reached their proper audience sooner and with less trouble to all. Librarians should not feel themselves to be under any obligation to buy this bundle of mainly ephemeral reports merely because it is held between hard covers. *D. B. Spalding*

FOREST PATHOLOGY

Pathology of Trees and Shrubs, with Special Reference to Britain, *by T. R. Peace. Pp. xx+723 +16 plates. Clarendon Press; Oxford University Press, London. 1962. 90s. net.*

This book summarizes the life-work of the author, who, at the time of his death in 1962, was the Chief Research Officer of the Forestry Commission. It is an authoritative work on diseases of temperate forest trees and ornamental trees and shrubs caused by fungi, bacteria, viruses, and by non-living agents. It is well illustrated by just over a hundred excellent line drawings and sixteen plates, and there is a most comprehensive bibliography of about 2500 references. The fact that it has been written with special reference to diseases and conditions in Britain does little to reduce its value to workers elsewhere, because each of a wide range of subjects is dealt with thoroughly and comprehensively. The value of this book to the specialist concerned with teaching and research in forest pathology goes almost without saying, but it has been written so that it will also meet the less specialized needs of foresters. There can be little doubt that the book will rapidly become established as one of the major works of reference on forest pathology in the English language, and it is a matter of great regret that the author died before he could receive the acclaim that will follow its publication. *R. K. S. Wood*

HISTORY OF SCIENCE

The Collected Papers of Lord Rutherford of Nelson, ***under the scientific direction of Sir James Chadwick. Vol. I,*** **New Zealand, Cambridge, Montreal.** ***Pp.*** **931.** ***George Allen and Unwin Ltd, London.*** **1962. £6 6s. net.**

The publication of the collected papers of Lord Rutherford under the scientific editorship of Sir James Chadwick commemorates something unique in history—the development of a whole branch of learning displayed in the work of a single man. Of course, others did important work in the discovery and elucidation of radioactivity, but the systematic theoretical development was carried out by Rutherford, with the remarkable clarity of thought that stands out from the written papers.

The volume covers his work from 1894 until he left Montreal in 1907. It begins with papers on the magnetic effect of high-frequency currents, and continues with work on gaseous ionization inspired by J. J. Thomson. From the first, he showed great skill in devising experiments and masterly clarity in interpreting them, but one feels that the standard could have been attained by many first-class young workers. Rutherford's real life-work began within a few months of his appointment to Montreal, when he started work on the production of new radio-elements from thorium and uranium. This radioactive transformation—nuclear chemistry—is the burden of most of the papers in this volume. Towards the end of the series we find the beginnings of nuclear physics. Rutherford in 1907 began to speculate on the relation of the energy of the α-particles to the lifetime of the nuclei that emit them. Beginning in 1902, he had ideas on the radioactive heating in the Earth, and before the end of the period he had established radioactivity as an essential factor in geophysics and as a basis for geochronology.

The book contains a number of plates and appreciative notes by Chadwick, Appleton, Bronson, and Hahn. *H. J. J. Braddick*

A History of Chemistry, ***Vol. III, by J. R. Partington. Pp. xxiv+854. Macmillan & Co. Ltd London; St Martin's Press, New York. 1962. £6 6s. net.***

This third volume, the second to appear, of Professor Partington's four-volume history of chemistry continues the encyclopaedic treatment of Volume II in what may be for some readers an even more interesting period, that from about 1700 to 1800. The first three chapters deal, however, with French chemistry from 1600, rather than from 1700, and continue to 1800, with the work of Lavoisier set apart for a separate and later chapter. Then follow three chapters, one on Hales and Black and two on chemistry in Scandinavia. The three succeeding chapters are separately concerned with three great figures in eighteenth-century chemistry, Priestley, Cavendish, and Lavoisier. The next two chapters deal with Lavoisier's contemporaries and immediate successors in France. Then a chapter is devoted to chemistry in Germany during the period under review. Further chapters on the later phlogiston theory, on the foundations of stoichiometry, on chemistry in Great Britain and Ireland, on Bryan and William Higgins, and on Dalton complete this extensive study. As before, there are exhaustive documented biographies with bibliographies for every chemist discussed, and name and subject indexes together with 71 illustrations. This is an invaluable reference work for historians of chemistry. *Douglas McKie*

Alfred Nobel, the Man and His Work, ***by Erik Bergengren (translated by Alan Blair). Pp. xviii+222. Thomas Nelson & Sons Ltd, Edinburgh. 1962. 30s. net.***

In the preface that he wrote for the original Swedish edition of this book, the chairman of the Nobel Foundation explains that the author has been given access to their archives in order to produce a 'straightforward account of Nobel, his achievements, and his will'. Some of the material has not been used by earlier biographers—notably the rather pathetic story of the relations between this lonely and unhappy man of genius and the youthful Viennese Jewess who exploited his wealth to the full. The account of his business enterprises and of the inventions on which they were founded also has an unusual degree of clarity. But the general effect on the reader is to make him wish for a bigger book, which might enable us to do justice to Alfred Nobel as the pioneer that he was, not merely in the field of explosives—though the opening up of natural resources in the later nineteenth century would have been appreciably slower had he not lived and worked as he did—but in the application of the scientific mind to the central problems of world politics.

In 1876 Nobel was thinking in terms of an explosive as a deterrent. Fourteen years later, in a discussion with Schneider of Le Creusot, he is said to have expressed the view that the effect of explosives was too restricted to deter mankind from war: 'All war will stop instantly, if the weapon is bacteriology'. *T. K. Derry*

Nobel, the Man and his Prizes, ***edited by the Nobel Foundation (second revised enlarged edition). Pp. x+690. Elsevier Publishing Co., Amsterdam. 1962. 60s. net.***

Although each year the award of the annual Nobel Prizes is given wide publicity, knowledge of their origin and of Alfred Nobel, who created them, is much less widespread. This is surprising, as a study of the prize awards since their inception in 1901 provides a remarkable commentary on the progress of the subjects concerned during this century. In 1950 the Nobel Foundation, to mark the completion of fifty years since its foundation, produced 'Nobel, the Man and his Prizes', a remarkable book in which these matters are covered in a series of articles written, in the case of the general and biographical parts, by friends and associates of Alfred Nobel, and, in the historical review of each prize, by eminent Swedish academicians. It has now been revised and enlarged so as to give an account of the prizes up to and including the awards for 1961.

The history of each of the five Nobel prizes is dealt with in considerable detail. For example, the limitations imposed upon the adjudicators by the terms of Alfred Nobel's will are recorded, as well as the manner in which they endeavour to carry out their difficult task of selection. And, viewed as a whole, it must be admitted that during the years of their existence the awards have maintained a remarkable standard of impartiality which has maintained their reputation. Of especial interest to the scientific reader are the accounts of the early awards in physics, chemistry, and medicine, and the reasons for the omission of certain names well-known in science at that time. *Lord Todd*

SCIENTIFIC BIBLIOGRAPHY

Scientific Books, Libraries and Collectors. A Study of Bibliography and the Book Trade in relation to Science ***(completely revised edition), by John L. Thornton and R. I. J. Tully. Pp. xiii+406. The Library Association, London. 1962. 68s. net. (51s. to Library Association Members).***

The first edition of this book, which deals with scientific books and libraries, and with scientific societies so far as they act as publishing agents, from their earliest times to the present day, appeared in 1954 and met with a deserved welcome. It was reprinted in 1956 and now appears in a revised and very much enlarged form, the original number of pages having been increased by more than a third. Checking at various points shows that the matter has been brought up to date: for instance, an article by Koyré and Bernard Cohen, published in 1961 on a Newtonian question, is included in the excellent bibliography. The book is of great value, not only to librarians concerned with scientific books, but also to historians and collectors. Its utility is enhanced by an admirable index.

As an indication of the percipience and independent judgment of the authors the following quotation, from the new matter added to the chapter on the growth of scientific periodical literature, may serve. After referring to the fact that certain publishers are issuing streams of new journals on every conceivable subdivision of science, they write: 'Publication is encouraged: the use of grants must be justified by the number of articles printed, and the work of a university department tends to be judged by the weight of its literary output. We are faced with a gigantic suicidal pact, in which the advancement of science is hampered by the inability of research workers to trace new facts among the masses of literature that must eventually suffocate those in pursuit of true knowledge.' The authors are not men of science, but probably few men of science will dispute their opinion on this matter. *E. N. da C. Andrade*

Some books received

(*Note.* Mention of a book on this page does not preclude subsequent review.)

MATHEMATICS

Guide to the Applications of Laplace Transforms, *by Gustav Doetsch (translation editor: W. McA. Fairbairn). Pp. 255. D. Van Nostrand Co. Ltd, London. 1963. 45s. net.*

The USSR Olympiad Problem Book. *Revised and edited by Irving Sussman (translated by John Maykovich). Pp. xvi+452. W. H. Freeman & Co. Ltd, San Francisco and London. 1962. 63s. net.*

Via Vector to Tensor, *by W. G. Bickley and R. E. Gibson. Pp. xvi+152. The English Universities Press Ltd, London. 1962. 21s. net.*

ASTRONOMY

Advances in Astronomy and Astrophysics. *Edited by Zdeněk Kopal. Vol. I. Pp. x+366. Academic Press Inc., New York and London. 1962. 80s. net.*

The Discovery of Neptune, *by Morton Grosser. Pp. 172. Harvard University Press, Oxford. University Press, London. 1962. 40s. net.*

Monde von Menschenhand, *by Werner Büdeler. Pp. 223. Union Verlag, Stuttgart. 1962. DM 12,80.*

PHYSICS

Elementary Particles and Cosmic Rays, *by Alladi Ramakrishnan. Pp. xvi+567. Pergamon Press Ltd, Oxford. 1962. £5 net.*

Eléments de thermodynamique statistique, *by A. Pacault. Pp. xv+358. Masson et Cie, Paris. 1963. 46 F.*

Geometrical Optics, *by W. T. Welford. Vol. I. Pp. x+200. North-Holland Publishing Co., Amsterdam. 1962. 35s. net.*

Introduction à l'électrodynamique quantique, *by Daniel Kastler. Pp. xxxiii+333. Dunod, Paris. 1961. 68 F.*

An Introduction to Tensor Calculus and Relativity, *by Derek F. Lawden. Pp. xii+172. Methuen & Co. Ltd, London; John Wiley & Sons Inc., New York. 1962. 25s. net.*

Light, *by R. W. Ditchburn (second edition). Pp. xxvi+833. Blackie & Son Ltd, London and Glasgow. 1963. 75s net.*

Non-equilibrium Thermodynamics, *by S. R. de Groot and P. Mazur. Pp. x+510. North-Holland Publishing Co., Amsterdam. 1962. 90s. net.*

Operational Methods for Linear Systems, *by Wilfred Kaplan. Pp. xi+577. Addison-Wesley Publishing Co. Inc., Reading, Mass., and London. 1962. 59s. net.*

Quantum Mechanics, *by Sin-Itiro Tomonaga (translated from the Japanese by Koshiba). Vol. I. Pp. xii+313. North-Holland Publishing Co., Amsterdam. 1962. 70s. net.*

Viscosity and its Measurement, *by A. Dinsdale and F. Moore. Pp. v+67. Chapman and Hall Ltd, London, and Reinhold Publishing Corporation, New York (published on behalf of the Institute of Physics and the Physical Society). 1962. 7s. 6d. net.*

CHEMISTRY

The Analytical Chemistry of Indium, *by A. I. Busev (translated from the Russian by J. T. Greaves). Vol. 5. Pp. xi+288. Pergamon Press Ltd, Oxford. 1962. 84s. net.*

Chemie im Dienst der Archäologie, Bautechnik, Denkmalpflege, *by J. Arvid Hedvall. Pp. x+226. Akademiförlaget-Gumperts, Gothenburg. 1962. 95 Sw. Kr.*

Les cyclitols: chimie, biochimie, biologie, *by Th. Posternak. Pp. 492. Hermann, Paris. 1962. 48 F.*

Gas Chromatography, *by John H. Knox. Pp. viii+126. Methuen & Co. Ltd, London. 1962. 15s. net.*

Nouveau traité de chimie minérale. *Edited by Paul Pascal. Vol. XV, part III. Paper bound, 180 F; cloth bound, 192 F. Vol. XX, part I. Paper bound, 134 F; cloth bound, 146 F. Masson et Cie., Paris. 1962.*

Organic Chemistry, *by D. J. Waddington. Pp. x+442. Mills and Boon Ltd, London. 1962. 22s. 6d. net.*

Organic Chemistry: An Introduction, *by M. F. Grundon and H. B. Henbest. Pp. viii+208. Oldbourne Press, London. 1962. 22s. 6d. net.*

Progress in Nuclear Energy, *Series IX,* Analytical Chemistry, *Vol. 3, Parts 1–3, edited by C. E. Crouthamel. Pp. 93. Pergamon Press, Oxford. 1962. 30s. net.*

PALAEONTOLOGY

Problèmes actuels de paléontologie. *Pp. 474. Centre National de la Recherche Scientifique, Paris. 1962. 62 F.*

BIOLOGY

Biological Transport, *by Halvor N. Christensen. Pp. viii+133. W. A. Benjamin Inc., New York. 1962. $6.50.*

Deoxyribonucleic Acid – Structure, Synthesis and Function. *Pp. ix+235. Pergamon Press Ltd, Oxford. 1962. 60s. net.*

Fish as Food. *Edited by G. Borgstrom. Vol. II. Pp. xvii+777. Academic Press Inc., New York and London. 1962. 178s. 6d. net.*

The Ideas of Biology, *by J. T. Bonner. Pp. 240. Eyre and Spottiswoode, London. 1963. 21s. net.*

Mutation: An Introduction to Research on Mutagenesis, *by C. Auerbach. Pp. xii+176. Oliver and Boyd Ltd, Edinburgh. 1962. 12s. 6d. net.*

Proving Ground, *by Neal O. Hines. Pp. xvii+366. University of Washington Press, Seattle 5, Washington. 1963. $6.75.*

Survey of Biological Progress. *Edited by Bentley Glass. Vol. IV. Pp. xiii+465. Academic Press Inc., New York and London. 1962. 80s. net.*

Viruses, *by K. M. Smith. Pp. 134. Cambridge University Press, London. 1962. Cloth, 21s. net; paper, 12s. 6d. net.*

ZOOLOGY

A Biology of Dragonflies, *by P. S. Corbet. Pp. xvi+247. H. F. & G. Witherby Ltd, London. 1962. 30s. net.*

Bird Flight, *by K. Simkiss. Pp. 96. Hutchinson Educational Ltd, London. 1963. 12s. 6d. net.*

Echinoderms, *by D. Nichols. Pp. 200. Hutchinson & Co. (Publishers) Ltd, London. 1962. 12s. 6d. net.*

A History of Domesticated Animals, *by F. E. Zeuner. Pp. 560. Hutchinson & Co. (Publishers) Ltd, London. 1963. 84s. net.*

Missions dans le Pacifique, *by G. Ranson. Pp. vii+97. Paul Lechevalier, Paris. 1962. 20 F.*

Soil and Freshwater Nematodes, *by T. Goodey, revised by J. B. Goodey. Pp. xvi+544. Methuen & Co. Ltd, London. 1963. £5 net.*

Spermatozoan Motility. *Edited by D. W. Bishop. Pp. viii+313. Bailey Bros. and Swinfen Ltd, London. 1962. 75s. net.*

MEDICINE

Comparative Neuropathology, *by J. R. M. Innes and L. Z. Saunders. Pp. xx+839. Academic Press Inc., New York and London. 1962. 229s. net.*

Diseases of Porphyrin Metabolism, *by A. Goldberg and C. Rimington. Pp. xvi+231. Charles C. Thomas, Springfield, Illinois. 1962. $9.75.*

The General Infirmary at Leeds, *by S. T. Anning. Vol. I. Pp. xii+107. E. & S. Livingstone Ltd, Edinburgh and London. 1963. 30s. net.*

Histologie und mikroskopische Anatomie des Menschen, *by W. Bargmann (4th edition, revised). Pp. xv+841. Georg Thieme Verlag, Stuttgart. 1962. 72 DM.*

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Forest Influences. FAO Forestry and Forest Products Studies No. 15. *Pp. xix+307. Food and Agriculture Organization of the United Nations, Rome. 1963. 15s. net.*

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Acetal Resins, *by Russell B. Akin. Pp. xi+178. Reinhold Publishing Corporation, New York. Chapman and Hall Ltd, London. 1962. 50s. net.*

Benzoles: Production aud Uses. *Edited by G. Claxton. Pp. xiii+979. The National Benzole and Allied Products Association, London. 1961. £5 5s. net.*

Flight Mechanics, *by Angelo Miele. Vol. I. Theory of Flight Paths. Pp. xi+416. Addison-Wesley Publishing Co. Inc., Reading, Massachusetts and London. 1962. 75s. net.*

The History and Use of Diamond, *by S. Tolansky. Pp. 166. Methuen & Co. Ltd, London. 1962. 30s. net.*

The Metal Plutonium. *Edited by A. S. Coffinberry and W. N. Miner. Pp. xi+446. The University of Chicago Press, London. 1962. 76s. net.*

HISTORY OF SCIENCE

La vie et l'œuvre d'Etienne Geoffroy Saint-Hilaire, *by T. Cahn. Pp. 318. Presses Universitaires de France, Paris. 1962. 20 F.*

[The price of 'Particle Accelerators' by M. S. Livingston and J. P. Blewett, published by McGraw Hill Book Co. Inc., New York and London, which was reviewed in the last issue of *Endeavour*, is £6 15s. 6d. net and not £6 1s. 6d. net as stated.]

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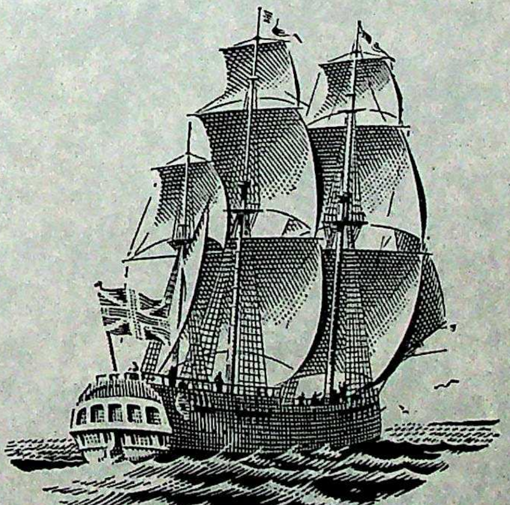

ENDEAVOUR

S. R. Bose.
11. 11. 63.

VOLUME XXII NUMBER 87 SEPTEMBER 1963

Endeavour

Endeavour has been published by Imperial Chemical Industries since 1942. It presents, for scientists throughout the world, a regular review of the progress of science. While the emphasis is on British science, contributions are regularly commissioned from all parts of the world; the principal considerations are the intrinsic interest and importance of the subject and the authority of the writer. To ensure international acceptance, the journal is published in English, French, German, Italian, and Spanish.

No charge is made for *Endeavour*, and it is distributed to senior scientists, scientific institutions, and libraries throughout the world. Within these limits, the Editor is always glad to consider the addition of names to the mailing list.

The drawing on the cover is of the bark *Endeavour*, which, commanded by Captain James Cook and carrying a number of scientific workers, was sent out by the British Admiralty in August 1768, following a Memorial by the Royal Society to King George III, to chart the South Pacific Ocean and observe the transit of Venus.

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VOLUME XXII SEPTEMBER 1963

A review of the progress of science, published in five languages

Editor TREVOR I. WILLIAMS, M.A., B.Sc., D.PHIL., F.R.I.C.
Foreign Editor G.N.J. BECK, B.Sc., A.M.I.E.E.
Assistant Editor W. A. OSMAN, B.Sc., M.Sc., A.R.C.S.

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Transatlantic science traffic

Although science traditionally acknowledges no frontiers of race or language, there has been much disquiet at the recent revelation of the extent to which scientists of many countries are emigrating to the United States. That this has long been going on is well known, but it is only comparatively recently, with the publication of reports by the National Science Foundation[1] in Washington and the Royal Society[2] in London, that the full extent of the trend has been made clear. There is likely to be no immediate slackening of the tide. The National Science Foundation report points out that the United States is traditionally an immigrant country; that the influx of foreign scientists has broadened the outlook of American-born ones; and that American institutions of higher education do not provide sufficient scientists for present needs.

During 1949–61, covered by the National Science Foundation, no fewer than 43 523 qualified engineers and scientists were admitted to the United States as immigrants, that is, as aliens admitted for permanent residence. Of these, about 10 000 were natural scientists, more than half of them (about 6000) chemists; physicists numbered 1089, and biologists 419. They came from all parts of the world, with Canada and the United Kingdom heading the list and Germany close behind. Many of the smaller countries of Europe have contributed relatively large numbers. For example, in 1961, the last year for which figures are available, the total number of immigrant engineers and scientists was 3922 compared with 5823 in the peak year of 1957. Of these, 1040 came from Canada, 575 from the United Kingdom, 291 from Germany, 108 from Holland, 102 from Switzerland, 73 from Sweden, 58 from France, and 49 from Italy. In proportion to size of population, the loss from Holland and Sweden is roughly the same as from the United Kingdom; from Switzerland, it is almost twice as great. By contrast, the relative loss from Western Germany is low, barely half that from Britain. The Asian countries as a whole contributed 336.

The figures alone do not indicate the full strength of the tide, for there is good evidence that those admitted as immigrants are of above-average ability. For example, 17·3 per cent of the members of the National Academy of Sciences and 37·5 per cent of Nobel Laureates in the United States are foreign born and foreign trained. Both figures are disproportionately large, for it is believed that immigrants do not account for more than 10 per cent of the American scientific manpower pool. However, this sort of situation is not peculiar to the United States. In Britain, for example, some 64 of the 600 Fellows of the Royal Society are immigrants.

The Royal Society's report both complements and supplements that of the National Science Foundation, for it deals with the emigration of scientists from Britain not only to the United States but to other countries. The inquiry was concerned with men of Ph.D. standard or better, and indicates that the annual rate of permanent emigration of scientists and engineers is about 140 per annum, representing about one-eighth of the country's total output. This must, however, be very much a minimal figure, as relatively few engineers take Ph.D. degrees in Britain; this is borne out by the National Science Foundation figures. But rather less than half the total from Britain go to the United States; some 55 go each year to Commonwealth countries, especially Canada, though for many the latter is a stepping-stone to the United States. The loss is particularly great in chemistry and physics—over the last decade, the numbers were 364 and 206 respectively, out of a total of 1136. While the greater number of those emigrating are young men, the loss of senior men also is considerable.

For Britain, as for other countries concerned, this is a serious matter. The cost of educating the men in question is not easily computed, though it is said that in Britain every Ph.D. graduate represents an investment of about £20 000 of public money. The cost to Britain of all the scientists and engineers lost to the United States during the last decade must be at least £23 million on the Royal Society's figures, and a great deal more if the National Science Foundation's statistics are used. More serious, in the opinion of the Royal Society Committee, are 'the economic consequences of the loss . . . of the leadership and the creative contributions to science and technology which they would have made in the course of their working lives'.

Neither report attempts to assess the reasons for this steady flow of scientists to the United States. Nevertheless, it seems clear that, at least so far as the United Kingdom is concerned, and probably for most other countries, there are two dominant factors: firstly, better research facilities and, secondly, higher salaries. If so, the remedy is clear, if not necessarily practicable. For some countries it is at present manifestly impossible to match the salaries and conditions of scientists in the richest and technologically most advanced country in the world. For others, especially those of western Europe, it is not necessarily impossible, and their governments would do well to ponder how their policy towards science and technology should be changed in order to avoid this steady and damaging drain from their ablest men. Financial considerations involved in the case of chemists have lately been analysed in some detail.[3]

However, it would be quite wrong to ignore the other side of the picture, and leave out of account the United States' own contribution to world science. If we are sincere in our belief in the internationalism of science, we should rejoice at the prospect of good research well done, regardless of who does it or where. The only reservation should be that results are freely published, for the use of all.

America continues her tradition of offering asylum to refugees. For example, of the 200 000 Hungarians who fled from their own country after the revolution of 1956, some 38 000 had reached the United States by mid-1958. Of these, 2000 were scientists and engineers, most of whom have now found appropriate professional employment there. Again, although the United States retains many of the foreign scientists who go to work there, a large proportion return to their own countries all the better for their experience.

It must not be forgotten, either, that the United States—both through its government agencies and its great charitable foundations—spends very large sums indeed on supporting research abroad. It is stated[4] that U.S. government expenditure overseas on research and development was $74 million in 1961—of which about one-third was for basic research—and the whole is expected to rise to $98 million this year. The greater part of this has hitherto gone to Europe, though the proportion allocated to Asia is steadily increasing. American research workers, too, are familiar—and welcome—visitors in laboratories in many parts of the world; the regrettable thing is that, for essentially practical reasons, it is rare for them to take up permanent posts abroad. If they did, and a kind of dynamic equilibrium were established, there would be no need for the present concern about the movement of scientists towards the United States.

[1] Scientific Manpower from Abroad: United States Scientists and Engineers of Foreign Birth and Training. 1962.

[2] Emigration of Scientists from the United Kingdom: Report of a Committee appointed by the Council of the Royal Society. 1963.

[3] Report on Chemists' Salaries in the United States. Braunsberg, H. *J. Roy. Inst. Chem.*, 87, 227, 1963.

[4] Federal Funds for Science XI: Fiscal Years 1961, 1962, 1963. National Science Foundation, 1963.

Atherosclerosis

Sir Howard Florey

This article shows how a chronic disease of widespread distribution is being investigated by the accumulation of data from observations on man and his environment, and by biochemical investigations on man where this is possible, on animals as a substitute for man, and *in vitro*. These investigations are coupled with the use of the most modern histological and microscopical techniques. At present, the greatest need seems to be a clearer understanding of the nature of thrombosis.

The greatest advances of medicine during the last century have been in the realm of infectious disease. These successes were based upon the fundamental discoveries by Pasteur, Koch, and others of the relation of micro-organisms to disease processes. Many chronic diseases, of which arterial disease is one, have not as yet been shown to have any comparable unifying thread to connect them. They are at the stage of examination by the collection of data from whatever source they can be gleaned.

One such disease is coronary thrombosis, or what is commonly called a 'heart attack'. It is now a common cause of death, and it is also of some considerable importance as a cause of disability.

Some views about its causation have gained wide publicity, although the 'facts' on which they are based are by no means universally accepted as true. One such popular opinion is that fats and cholesterol are the cause of the disease, but the relationship is not firmly established.

It is believed by pathologists at the present time that a disease of the arteries, commonly known as atherosclerosis, underlies the process of coronary thrombosis. That such a disease is not exclusively a by-product of modern civilisation is shown by the fact that fragments of the aorta from Egyptian mummies dating from between 1500 B.C. and A.D. 525 show typical lesions. One of the earliest descriptions of the disease was that of the aorta of a famous anatomist, J. J. Wepfer, who died in 1695 at the age of seventy-five. The accompanying picture of his aorta has a somewhat macabre association, for it was published in a posthumous edition of Wepfer's own anatomical observations (figure 1).

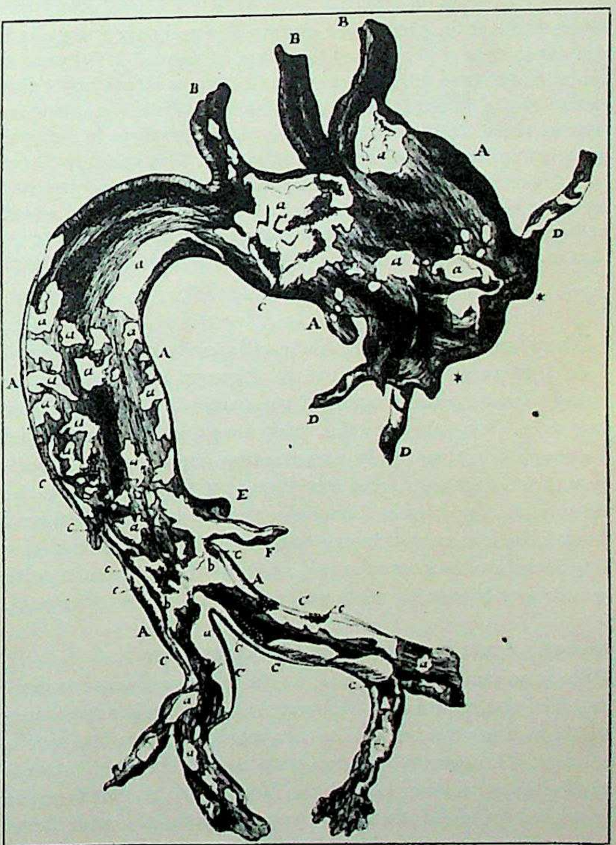
Certain facts about the disease have slowly accumulated during the past two hundred years. Thus in 1770, Edward Jenner, famous for his introduction of vaccination against smallpox, first noticed the connection between certain pains in the chest and a narrowing of the arteries supplying the heart. In 1850, the French anatomist Jean Cruveilhier connected disease of the arteries of the heart with alterations in the blood which led to the obliteration of the arterial lumen.

The modern investigation of the disease has centred on changes in the arterial wall, changes in the blood resulting in the deposition of solid matter, and the possible relationship between the two.

The arterial wall

The wall of a normal artery, such as one of the coronary vessels that supply the heart, consists of an inner lining of flattened cells, called endothelium, which adhere to a tissue consisting of mucopolysaccharides in which are interwoven fibres of collagen and elastic tissue. This internal layer, known as the intima, lines the main pressure-resisting layer of the vessel known as the media, which consists of elastic tissue, collagen fibres, and smooth muscle cells. External to this, there is an adventitia that consists of small blood vessels and fibrous tissue (figure 2).

The changes leading to well-developed atherosclerosis take place in the intima just subjacent to the endothelial lining. The precise nature of the initial changes still escapes detection, for even the electron microscope has so far not revealed anything of a striking nature. Features of the fully developed disease are, however, easy to recognize. The obvious lesion of atherosclerosis is thickening of the arterial intima due to the formation of new collagen fibres and elastic tissue, an increase



A.A.A.A. *Aorta inciſa & aperta tota interior facies conſpicitur.*
* * *Ejuſdem exortus.*
B.B.B. *Arteria caput petentes, ſeu carotidum &c. exortus.*
C.C.C. *Arteria iliaca.*
D.D.D. *Coronaria arteria.*
E. *Arteria cœliaca.*
F. *Arteria renalis ſeu emulgens.*
a.a.a.a.a.a.a.a. *Oſſea ſubſtantia Aorta per portiones incerta figura & magnitudinis hinc inde conſpicuas.*
b.b.b.b. *Circulus ejuſdem plane oſſeus.*
c.c.c.c. *Tunica interior lacera atque fracida, obſcuri coloris, non citra ruptionis periculum.*

Figure 1 Johann Wepfer's aorta, from his *Observationes Medico-Practicae de Affectibus Capitis Internis et Externis* (1727).

Sir Howard Florey, ***P.R.S., F.R.C.P.***
Was born in Adelaide in 1898 and is a graduate of the University of Adelaide. From 1935 to 1962 he was Professor of Pathology at Oxford University, and is now Provost of the Queen's College, Oxford. For his work on penicillin he was awarded a Nobel Prize in 1945. Since 1960 he has been President of the Royal Society.

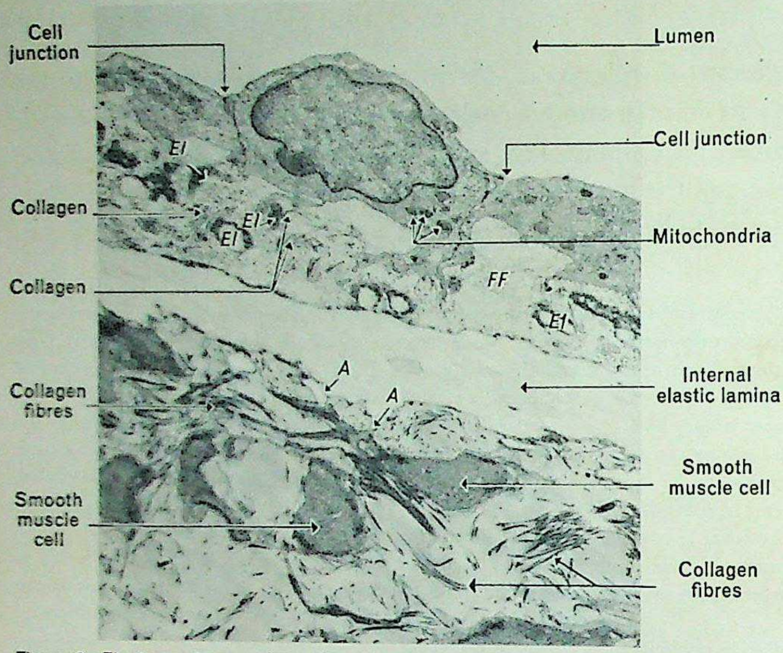


Figure 2 Electron micrograph section of a coronary artery of a young pig. The luminal surface is lined by endothelium composed of flattened cells in close apposition at their edges. Beneath this layer is a zone containing collagen fibres, elastic tissue fibres *(El)*, and other fine fibres *(FF)*. The intima is bounded by the internal elastic lamina. Atherosclerosis first develops in the space between the endothelium and the internal elastic lamina. This space in pictures obtained with the light microscope appears as little more than a line. External to the internal elastic lamina, a part of the media is shown; this contains smooth muscle cells and collagen fibres. At *A* the smooth muscle cells are attached to the internal elastic lamina. (×6 800) (By permission of the Editor of the *British Medical Journal*.)

in the number of smooth muscle cells, and the deposition of lipid substances (figures 3 and 4). Changes also occur in the mucopolysaccharide content of the spaces between the fibres and cells. Not only does this thickening tend to constrict the lumen of the vessel, but its presence may encourage the deposition of solid material from the blood at the site, leading to the all too familiar disease of coronary thrombosis. The thickened intima, besides containing deposits of lipid, often in the later stages accumulates considerable amounts of calcium salts, with consequent hardening of the vessel wall in that part (figure 5).

Investigations on the causes of atherosclerosis

The prominent lipid material in the thickened areas is composed of cholesterol and cholesterol esters as well as phospholipids and glycerides. It has attracted attention for over a century. The theory has been propounded that the disease is produced by abnormalities in the blood lipids, so that these are deposited in the intima in excessive quantities after being released from combination with the lipoproteins of the blood. When not combined in lipoproteins, the lipids are relatively insoluble, and may therefore remain in the intima for an indefinite time.

To test these views, an enormous body of data has been collected on the concentration of cholesterol, the ratio of phospholipid to cholesterol, and the concentration of lipoproteins in human blood, in populations living in a wide variety of nutritional and environmental circumstances. These statistical studies tend to show that populations that have a low level of blood cholesterol have relatively little coronary thrombosis, and that low levels of blood cholesterol are associated with poor diets, especially diets with a low fat content. At the same time, many maintain that Western Man, on a rich diet, often has a high level of blood cholesterol because of his high fat intake. Whether this type of research will provide crucial clues about the cause of the disease remains to be seen, but up to the present no theory arising from these observations has received universal acceptance.

Other methods of investigation depend on the work of biochemists and physical chemists, who are investigating in great detail the composition of lipids met with in the body and in arterial lesions. Considerable interest has been aroused by the discussion of whether the chemical nature of the fatty acids in the fatty substances encountered in lesions of atherosclerosis is important. One school of thought maintains that the polyunsaturated fatty acids are all-important, and that a relative lack of these in the diet is the cause of the deposition of lipid in the arterial wall. Others, on what appears to be good evidence, deny that this is so. So far, a mass of statistical biochemical, and biophysical observations has not produced any satisfactory or agreed proof that excess of fat, or of any particular kind of fat, in the diet is the cause of the disease.

It may well be asked whether a crucial experiment could not be performed to demonstrate whether the level of cholesterol in the blood really is of prime importance in the development of arterial disease. Experiments which at a first glance would seem to have returned an unequivocal answer to this question were performed by Anitschkow fifty years ago. He fed very substantial amounts of cholesterol to rabbits, which normally

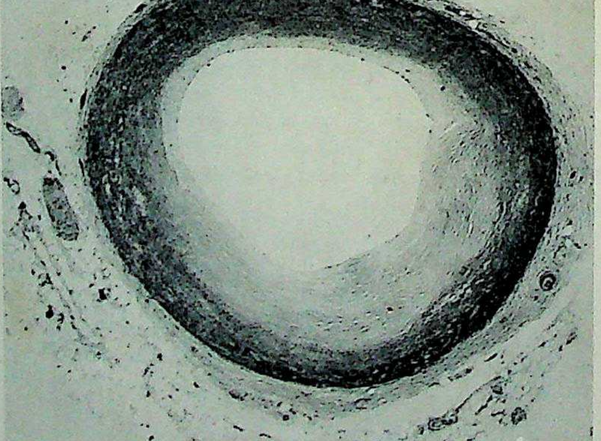
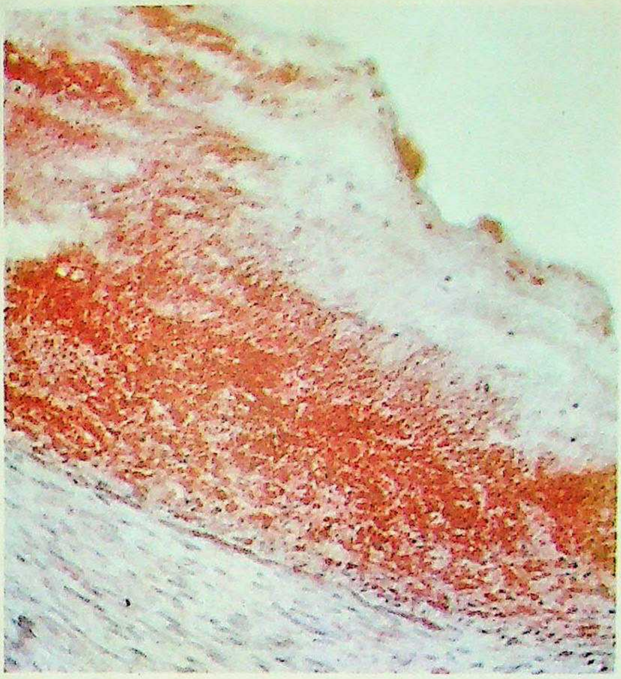


Figure 3 Cross-section of a human coronary artery to show thickening of the intima by atherosclerosis. The dark portion is the media and the lighter portion the thickened intima. (×18)



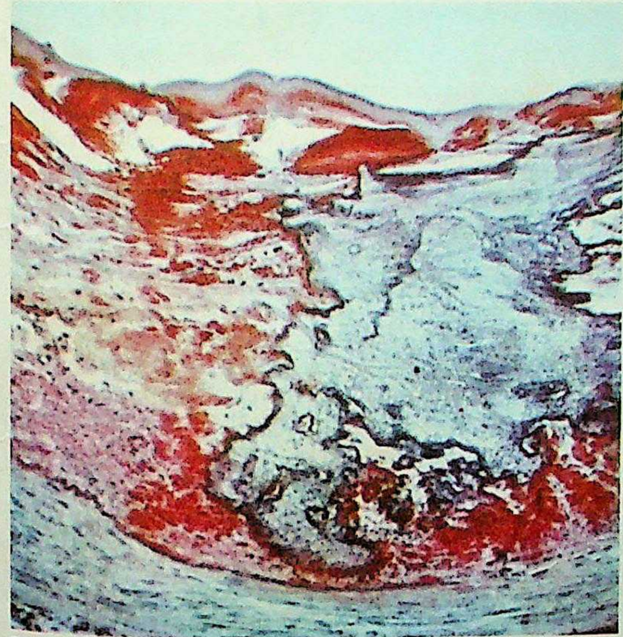


Figure 4 (above) Section of an atheromatous human coronary artery. Top right, part of the lumen of the vessel; bottom left, part of the media. Lipid, stained red, is spread throughout the thickened intima. Part of it is extracellular, but the denser portions are largely within cells—macrophages. (×96)

Figure 5 Section of an atheromatous human coronary artery. The lumen of the vessel is seen at the top and a small part of the media at the bottom. The thickened intima shows deposits of lipid (red) and of calcium salts (blue). (×96)

have a low level of cholesterol in the blood and a low intake of cholesterol from the foodstuff. With such treatment the level of the cholesterol in the blood rose to great heights, sometimes more than 1000 mg per 100 ml; this compares with a normal total cholesterol content of about 200 mg per 100 ml in human blood plasma, about one-quarter being uncombined. After weeks or months, the rabbits developed lesions in the arterial wall which bore some resemblance to those seen in the human disease, but these and similar experiments in other species suggest that the lesions produced are not identical with those seen in man. Nor, after many investigations, is it even clear precisely how the cholesterol in the blood is deposited in the arterial wall. In rabbits that have been given large quantities of cholesterol there is also a great accumulation of lipid in many other tissues and organs, especially the liver—a feature not encountered in man.

Some powerful support for the view that a high level of cholesterol in the blood determines the production of the lesions of atherosclerosis is furnished by the rare human disease known as familial hypercholesterolaemia. This disease is an inherited disturbance characterized by a high level of cholesterol in the blood, and is associated with severe atherosclerosis at an early age.

Arterial disease of animals

At the present time, the possibilities of comparative pathology are being explored by investigating whether the natural arterial diseases that occur in domestic and wild animals have any similarity to those of man. If a species could be found in which the lesions that occur spontaneously are, as far as can be ascertained, identical with those in man the way would be open to a more penetrating experimental study.

Some observations of great interest have been made during recent years on pigeons. It has been found that in a breed known as White Carneau, lesions occur in the aorta of all birds over three years old, and that these lesions bear a striking histological resemblance to those of atherosclerosis in man. But of further interest is the fact that while White Carneau pigeons develop lesions of this nature, other strains known as Show Racer and Racing Homer do not, even when fed on identical diets of grain and kept under the same conditions of housing and exercise. The occurrence of these susceptible and non-susceptible strains has enabled their discoverers to make a comparative study of the various factors which might be concerned in the development of lesions. Their differing susceptibilities cannot be attributed to differences in the cholesterol, phospholipid, or β-lipoprotein levels, for both susceptible and non-susceptible strains have what would be considered in mammals a high blood cholesterol, 300 or more mg per 100 ml. There is certainly a genetic element here, and at the present time a detailed search for possible inherited biochemical abnormalities is being conducted on this species, and an assessment of the influence of dietary factors on the development of the lesions is being made.

Recent investigations on the domestic pig have shown that it suffers from a disease that appears to be indistinguishable from the early stages of atherosclerosis in man. In my opinion, the way is open for the performance on this animal of some decisive experiments on the role of diet in the genesis and development of atherosclerosis. The pig resembles man in its omnivorous habits, and surpasses man in its ability to take diets of peculiar composition without complaint. It is indeed an excellent experimental animal for the exploration of dietetic factors. Such experiments might well resolve some of the problems that have been thrown up by the collection of data in man.

Other changes associated with atherosclerosis

While much attention has been concentrated on the behaviour of lipids, both in the arteries and in the body in general, it must not be forgotten that other components of the tissues are altered in arterial disease. For example, changes occur in the elastic tissue of the walls of the blood vessels very early in the development of atherosclerosis. It is not very many years since atherosclerosis was generally considered to be a natural part of the ageing process of the human body, and indeed it is well known that the disease is more frequent in the ageing than in the young. There is probably a good deal of substance in this idea, for it is difficult to believe that the elastic tissue of the arteries does not go through much the same changes as the elastic tissue of the skin. It is a familiar observation that as we get older our faces become wrinkled and tend to droop, and the skin on the backs of our hands becomes less elastic. Perhaps the changes in the elastic tissue of the arteries, easily observed by histological methods, are a manifestation of the same slow changes. Nevertheless, highly developed atherosclerosis can occur in quite young people, so that it seems right for the present to consider the arterial lesions as a real disorder of the tissues and not simply a result of ageing.

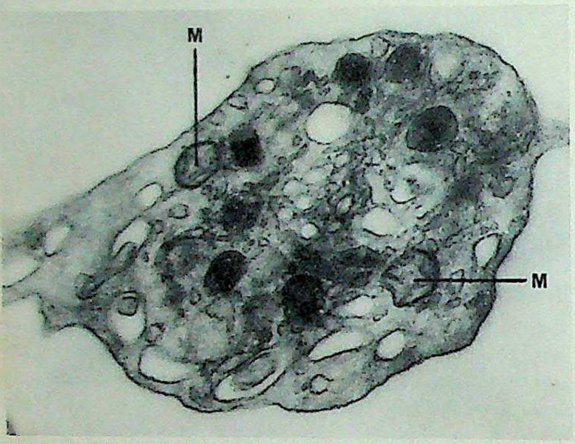


Figure 6 Platelet in lumen of a rat's blood vessel. Granules and vesicles can be seen, and mitochondria *(M)*. Electron micrograph by J. C. Hoak. (×47 000)

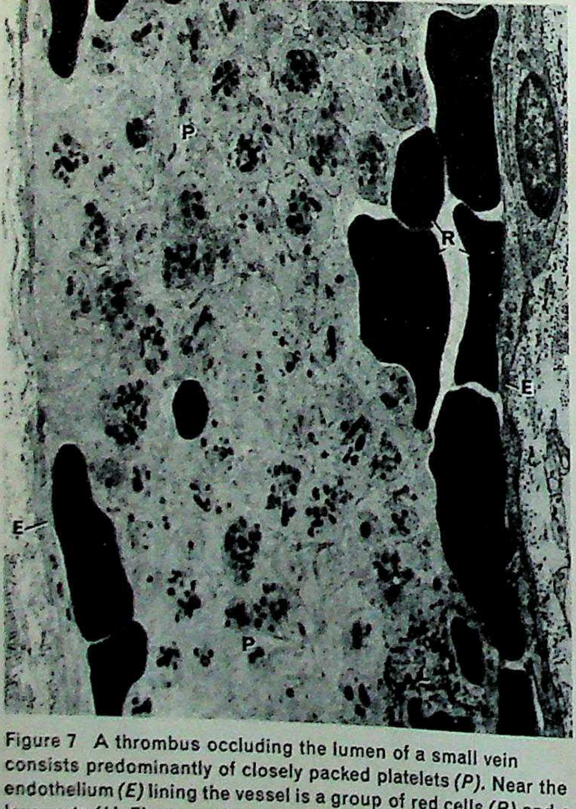


Figure 7 A thrombus occluding the lumen of a small vein consists predominantly of closely packed platelets *(P)*. Near the endothelium *(E)* lining the vessel is a group of red cells *(R)* and a leucocyte *(L)*. Electron micrograph by Dr J. E. French. (×7 000)

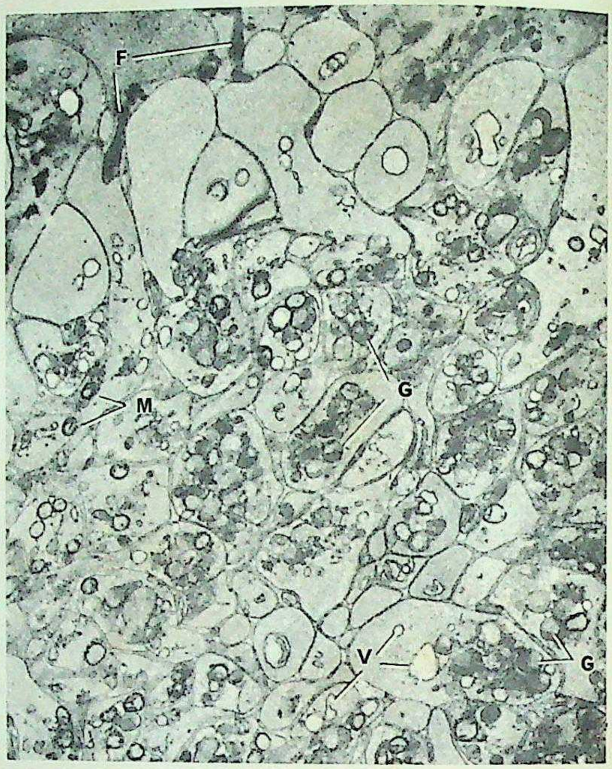


Figure 8 Agglutinated platelets, tightly packed together but retaining their limiting membranes. They contain granules *(G)*, mitochondria *(M)*, and vesicles *(V)* of various sizes. At the top of the picture the platelets have lost their granules, and some strands of fibrin *(F)* are seen between them. Permanganate fixation. Electron micrograph by Dr J. E. French (×12 800)

Atherosclerosis is not a disease that affects all arteries, or all parts of arteries, uniformly. It is patchy in nature, as can readily be seen in the aorta and coronary vessels. A completely acceptable explanation for this patchy distribution is still to be found, but it is possible that the mechanical strains induced in arteries by the pulsatile blood flow, with its sharp variations in pressure, may have an influence, but whether the changes in the elastic tissue are in any way related to repeated mechanical strains has not been conclusively shown.

There may well be changes in the mucopolysaccharides of the matrix in which the fibres of the intima are set, but methods for investigating these substances are as yet far from perfect, and no clear indication has been obtained that the origin of the disease is to be found in aberrations of the mucopolysaccharides. This is an active field of investigation at the present time.

It has long been known that women before the menopause are much less susceptible to coronary thrombosis than men of comparable age, but that with increasing age the rates in men and women tend to approximate. This observation has concentrated attention on whether female sex hormones may be responsible for the relative immunity of women. Attempts have been made to protect men who have already had a coronary thrombosis from further such episodes by administering appropriate female hormones. The results to date seem to show that possibly some slight advantage accrues from the procedure, but that the side effects, such as enlargement of the breasts and loss of libido, are not negligible.

Studies of the effects of other hormones, including those of the pituitary and thyroid glands, have not thrown any dazzling light on the causation of atherosclerosis.

The composition of the blood

Another possibility, now being vigorously investigated, may be of great importance in connection with the increase of coronary thrombosis in recent times. This concerns the composition of the blood. It is sometimes supposed that thrombosis, the blocking of a blood vessel by local solidification of the blood itself, is in all respects similar to the clotting of blood in a test tube. Nothing could be farther from the truth. Some one hundred and twenty years ago, small formed elements, much smaller than the red blood cells, and measuring some 2–3 μ in diameter, were detected in shed blood; they are now known by the name of blood platelets. Normally, platelets circulate in the blood as discrete bodies, but a thrombus, which is essentially an agglutination of platelets, can be formed from flowing blood by their deposition on the vessel wall. Subsequently fibrin, produced by the clotting mechanism from fibrinogen of the blood, and blood cells, such as the leucocytes and red cells, collect upon the platelets.

The electron microscope gives a very interesting and clear picture of the structure of platelets. They are found to consist of membrane-bounded material containing vesicles and granules, much like the cytoplasm of an ordinary cell but without a nucleus or endoplasmic reticulum (figure 6). When thrombosis occurs, the platelets become closely applied to one another, but the actual physical nature of their adhesion is unknown. It is certainly not due to dissolution of the platelets to form a structureless mass. The bounding membranes, at least at the beginning of the process, remain intact, though the granules are gradually discharged (figure 7 and 8).

Platelets are now known to contain considerable amounts of adenosine triphosphate, and it has recently been shown that adenosine diphosphate causes their agglutination. These observations have been carried one stage further, and it has been shown that adenosine, and to a lesser extent adenosine monophosphate, inhibit the agglutinating action of adenosine diphosphate, at least in some species. Noradrenaline and 5-hydroxytryptamine also agglutinate platelets, though less powerfully than adenosine diphosphate. Investigations of the properties of the platelets by biochemical means, correlated with observations in the electron microscope, are proceeding rapidly, and it is conceivable that in a few years we shall have a clear picture of what happens during the important process of thrombus formation.

There is no doubt that the process of thrombosis plays an important and sometimes dramatic part in the terminal stages of arterial disease by blocking a vessel already damaged by atherosclerosis. But it is thought to play an integral part also in the later stages of the development of lesions. Platelets and fibrin from the blood may be deposited on an atherosclerotic plaque forming a 'mural thrombus', and this may be incorporated into the plaque by being converted to fibrous tissue and receiving a covering of the normal lining cells of the vessel Successive thrombi may be incorporated in this way in layers and as they may become the site of lipid deposition, they may in the end be indistinguishable from the tissue of the diseased vessel wall.

There is little doubt that this process occurs, though it is not certain how large a part it plays in the development of lesions. What is much more debatable, though the suggestion has been vigorously revived recently, is whether the first stage of plaque formation is the deposition of platelets and fibrin on the vessel wall. Even if this were so, the initial change in the vessel wall which causes a thrombus to form at that point remains unexplained.

Perhaps from the medical point of view—that is to say in relation to disease of, in particular, the heart and brain—the central core of the problem is the understanding of thrombosis. At the present time investigations are in train to ascertain whether components of the blood such as fatty acids have an influence on the adhesiveness of blood platelets and hence possibly on their liability to form thrombi.

Acknowledgment

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A virus disease of a fungus: die-back of cultivated mushroom

M. Hollings, Doreen G. Gandy, and F. T. Last

Some of the disorders affecting mushroom crops can be corrected by altering the conditions of cultivation, and others are known to be caused by pathogenic fungi or bacteria that have been identified. There are, however, a number of disorders whose causes have for many years been unknown, and it has now been shown that some, and possibly most, of these are different manifestations of virus infection. This article describes the isolation of these viruses, and the criteria by which they were identified and shown to cause disease—the first known case of a virus infecting a fungus.

Many different fungi, such as Chanterelles, morels, and truffles, are prized as delicacies, but only *Agaricus* (*Psalliota*) *bisporus*, the common edible mushroom, is cultivated commercially in Europe. Some are grown in caves in France and the United States, but in Britain they are cultivated almost entirely in sheds and converted glasshouses in which temperature, atmospheric humidity, and the freshness of the atmosphere are controlled to differing degrees. Mushrooms are a crop of some importance, as the annual production in Britain is about 17 000 tons.

Colour variants of mushrooms are available as cultures, but white forms are usually grown. Mushroom growing is very much a skilled art rather than a science, and the timing of the various operations differs widely. Mycelium (spawn) is added to composted mixtures (usually horse manure plus additives) in trays or on shelves. After the spawn has grown sufficiently, the compost is covered with a shallow casing layer of soil, or peat and chalk. This stimulates fruiting, which occurs as a series of flushes at approximately weekly intervals. In Britain, when trays are used, the compost is cased approximately two weeks after spawning, and cropping starts three weeks later and lasts 6–10 weeks.

Mushroom crops are affected by several types of disorder. Some result from cultural conditions; others are caused by bacteria or by parasitic or competitive fungi. There is yet another group, the 'La France Complex', which includes La France disease, infectious Watery Stipe, Brown disease, and possibly Mummy disease, whose causes were until recently unknown, although viruses were suspected [10]. Circumstantial evidence led other workers to suggest that similar abnormalities of such wild 'toadstools' as *Laccaria* spp. [1], and of the oat parasite *Helminthosporium victoriae* [9] were also caused by virus. J. L. Jinks, however, considered that a growth decline of *Aspergillus glaucus*, similar to that found in the cultivated mushroom, was caused by lethal suppressive cytoplasmic genes [8].

Mushrooms develop a comparatively limited range of stalk (stipe) and cap (pileus) abnormalities in unfavourable conditions. Their tissues may become brown and leathery, or waterlogged and exude droplets as in Watery Stipe (figure 7), or granular as in Mummy disease (figure 8). Stalks may be excessively long in relation to the size of the cap, forming 'drumsticks', or the mushroom may remain stunted. Sometimes these symptoms are not associated with pathogens, and can be avoided in future flushes of the same crop by correcting physical conditions. The abnormalities of the La France group, however, are associated with the degeneration and death of the mycelium within the compost, reflected in the premature end to cropping. Sometimes the disease assumes epidemic proportions, causing large crop losses, as in England in 1957.

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Characteristics of the La France complex

Mycelia isolated from crops that could be restored to normal by changes in the physical environment showed no irregularities when grown on malt agar, but those from crops of white mushrooms that could not be restored, developed abnormally [2]. The diseased cultures grew more slowly than their healthy counterparts, were adpressed and not fluffy, and were without the usual development of coarse strands (figure 1).

When pure cultures of abnormal mycelia were inoculated to healthy crops, growth and cropping were affected. In experiments, cylinders of pasteurized compost were spawned at one end with healthy mushroom cultures and, after at least 16 days incubation, inoculated at that end with agar discs of diseased mycelium [4]. Colonization along the tubes was clearly visible as a pale grey weft, much reduced in the infected tubes (figure 2). In the first week, the linear growth increment of infected cultures was still 78 per cent of that of the healthy controls, but in the second week only 44 per cent (figure 3). When the inoculated ends were covered with a mixture of peat and chalk, mushrooms were consistently produced by the healthy series, but rarely by the diseased series.

In experiments done under commercial conditions, inoculating trays with either pure agar cultures or infected compost, at or before casing, usually caused a complete loss of marketable mushrooms—a few mis-shapen leathery ones sometimes developed. Delaying inoculation until the first 'pinheads' of the first flush appeared made the effects less dramatic; the causal agent seemed to spread less rapidly, and the effects on the yield were often difficult to detect (figure 4). Between these two extremes, however, intermediate stages were found. Thus when trays were inoculated seven days after casing, three distinct zones, arranged concentrically about the point of inoculation, showed at the first flush. A central zone with a few scattered deformed mushrooms was surrounded by a belt containing numerous undeveloped mushrooms that remained stunted and prematurely browned. This zone in turn was surrounded by an area of well-developed mushrooms some of which, near the stunted zone, exuded water from their stipes. As the crop aged, the barren area extended, with a consequent reduction in yield (figure 5).

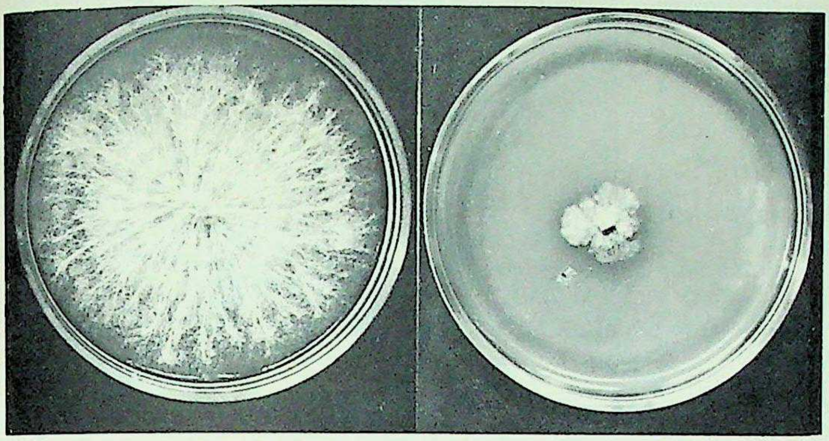


Figure 1 Growth of healthy (left) and virus-infected (right) mushroom cultures on malt agar after 28 days incubation at 25°C.

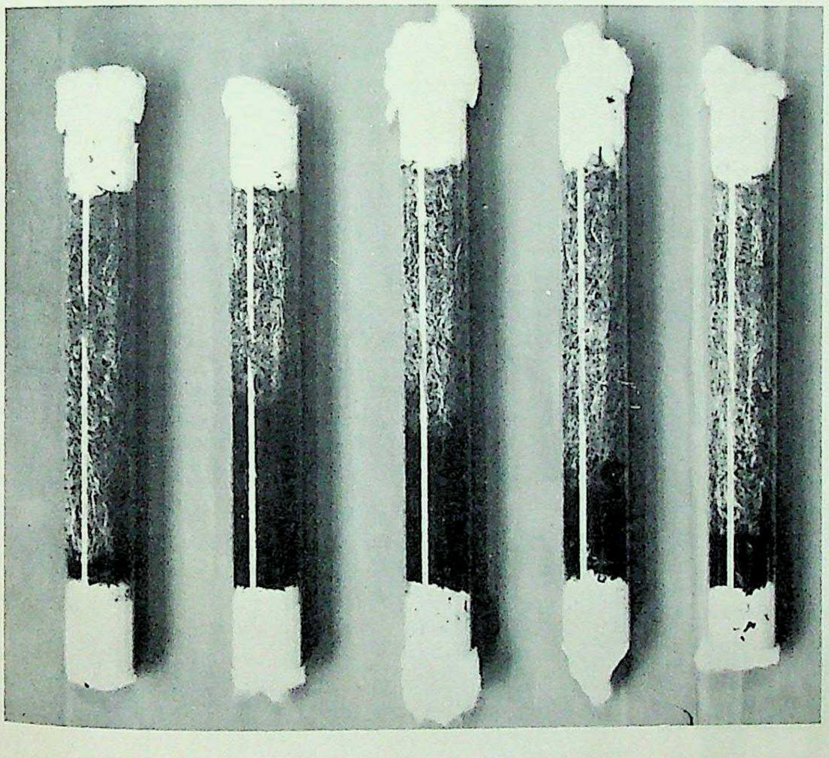


Figure 2 Effect of virus inoculations (diseased cultures) made at different intervals after spawning on hyphal growth along cylinders of compost; photograph taken six weeks after spawning. (From left to right: uninoculated control and tubes inoculated 16, 21, 28, and 35 days after spawning respectively.)

The effects described were all caused by pure cultures of abnormal mycelium. This, therefore, must carry the factor or factors responsible for damage. Little is known about the methods of transmission. However, anastomoses, networks of connections, were observed on agar media between abnormal hyphae and healthy hyphae that subsequently grew abnormally. This suggests that the infection is carried by a process akin to graft transmission. Agar cultures from single spores of healthy mushrooms are often atypical but, unlike those caused by an infectious principle, these variants are not transmitted by anastomoses. Further evidence pointing to the possibility of a virus as the causal agent was the restoration of diseased cultures to health when peripheral hyphae were subcultured after heat treatment at 33°C for two weeks. We then tried to isolate and purify any viruses present. None, of course, had been found in fungi at this time.

Virus purification

Hitherto, all our infections had been obtained with inocula containing living diseased cells; we now tried to find out whether cell-free preparations from diseased mushrooms contained virus-like particles, and whether these were responsible for the disease.

Two types of material were available: pure mycelial cultures, and mushrooms from cropping trays. Initially, we concentrated on the pure mycelial cultures in flasks and Petri dishes, to avoid contamination by other micro-organisms. The diseased mycelium grew so slowly that it was difficult to produce the bulk of material required, and no infection occurred when discs of healthy mycelium were dipped in preparations obtained after mechanically rupturing diseased tissue killed with cyanide. Consequently, attention was then turned to the sporophores, which offered a greater volume of material. These were at first collected from mushroom farms. Later, they were obtained by inoculating trays of mushroom spawn with infective compost.

The purification of viruses from flowering plants has usually involved maceration of infected material in suitably buffered liquids, to extract the virus and prevent its adsorption on to, or breakdown by, the other plant components. Plant fibre is removed by slow-speed centrifugation and the virus then sedimented by centrifugation of the clear supernatant fluid at

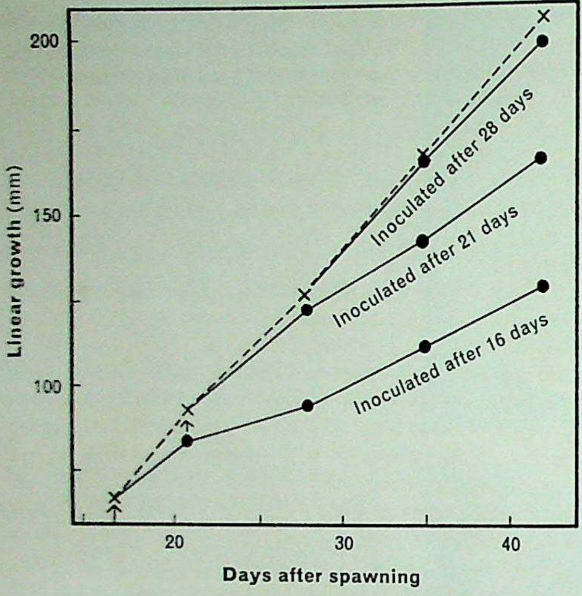


Figure 3 The linear growth of mushroom hyphae along cylinders of compost when inoculated with virus-infected cultures at different intervals after spawning (see figure 2). x - - x = uninoculated controls.

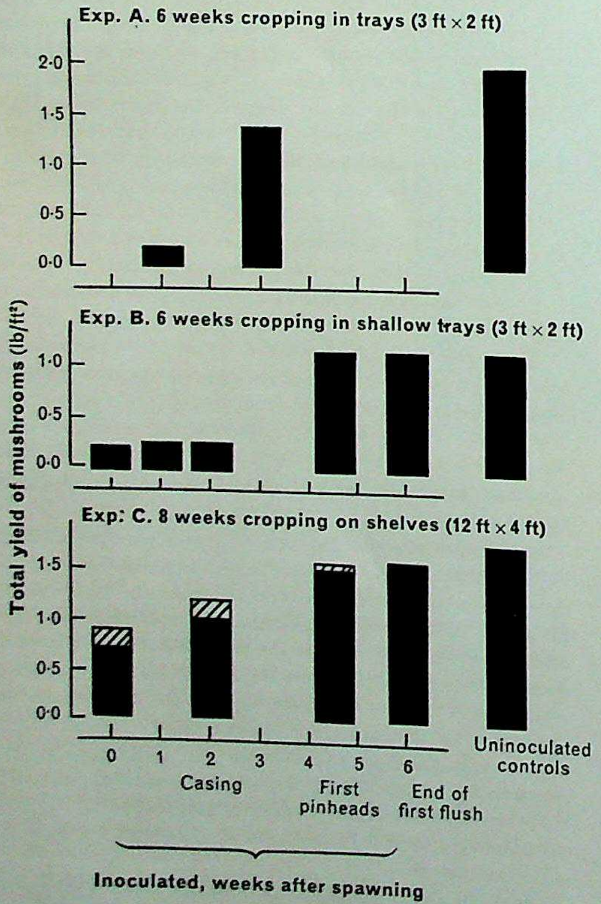


Figure 4 Effect of virus-infected cultures on mushroom yields when inoculated at different stages after spawning. (Cropping periods measured from the first pick, usually five weeks after spawning. (1 lb/ft² = 4·9 kg/m²). Abnormal mushrooms indicated by cross-hatching in Exp. C.)

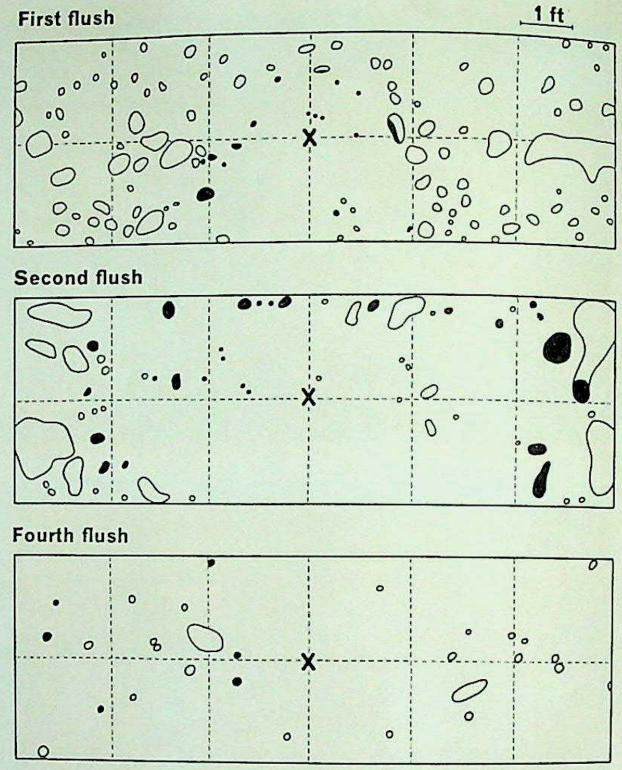


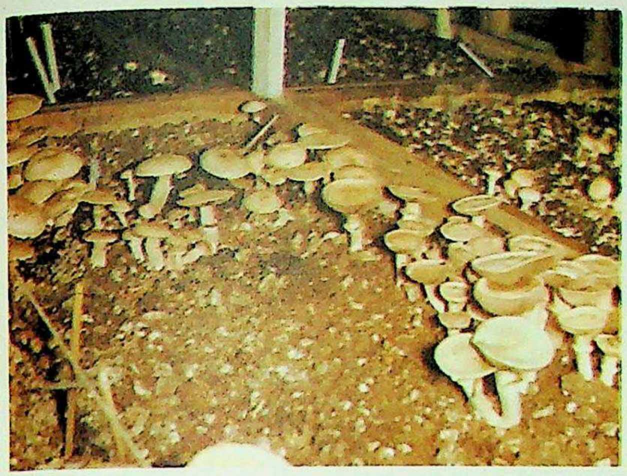
Figure 5 Effect of a virus-infected culture, centrally placed (x) at casing, on the cropping sequence of a previously healthy shelf crop of mushrooms. (First, second, and fourth flushes picked 27–32, 39–45, and 56–62 days after casing respectively. ○ = normal mushrooms; ● = abnormal mushrooms.)

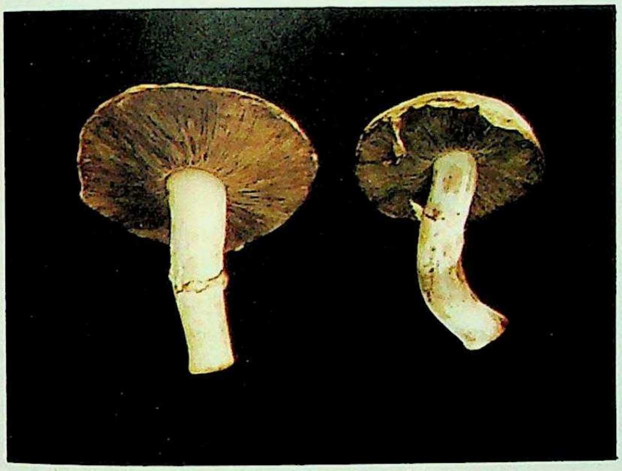
higher speeds. Although extraction methods that succeeded with several plant viruses gave a very low yield of mushroom virus and contained much unwanted host material [3], other extraction methods and fluids gave consistently good virus preparations without unwanted mushroom material [6].

Mushroom stalks were a better source of virus than the caps, and young sporophores were better than old. Further, the apparently normal mushrooms surrounding areas containing obviously diseased mushrooms were found to be symptomless carriers, and were a rich source of virus. Older sporophores contained less virus than the young ones, and the preparations from the older ones did not survive cold storage for even 24 hours. Later preparations, containing very little of the mushroom material, proved more stable and retained their properties for several weeks when stored between 0° and 2°C. Mushroom tissues are a rich source of phenol oxidase systems, which may be responsible for some of the virus inactivation.

We needed a means of quantitative assay of our virus preparations, and initially estimated the intensity of the visible zone produced in density-gradient centrifugation; this is a method used for some other viruses [7]. Centrifugation of virus preparations in transparent tubes containing gradient columns of sucrose solutions produced light-scattering zones, visible under suitable top illumination, at characteristic levels in the tubes. Later, the serological titre was used in quantitative assays. The yield of virus from different batches of material varied considerably, but, in general, the virus from 50 g of infective stipes, dispersed in 1 ml of buffer, gave good preparations.

Having found a method that would consistently produce satisfactory preparations, it was now necessary to see if our





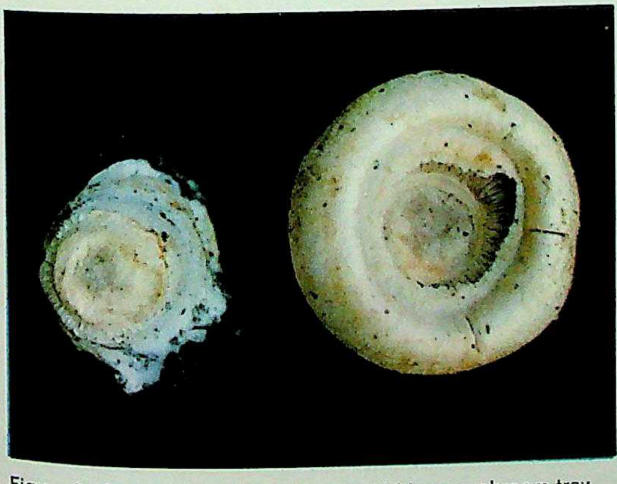


Figure 6 Spread of die-back disease within a mushroom tray, after inoculation in one corner (centre foreground). A zone of dwarf mushrooms is seen at the edge of the barren area, with unaffected mushrooms beyond.

Figure 7 Healthy (left) and virus-diseased (right) mushrooms of the same age. Note dark water-soaked lesion on bent stalk of diseased sporophore.

Figure 8 The broken ends of stalk (left) and cap (right) of a mushroom showing the central granular speckling characteristic of Mummy disease.

particles were viruses and whether they caused the disease. The criteria used for evaluating plant viruses are: (i) infectivity; (ii) the presence of characteristic particles in electron micrographs; (iii) specific serological activity; (iv) specific light-scattering zones when centrifuged in density-gradient columns; and (v) a specific ultraviolet absorption spectrum with a maximum in the 260 mμ waveband. This last would be confirmatory, as absorption at this frequency is typical of RNA.

Infectivity

Discs of healthy mushroom mycelium on agar were not infected when dipped in purified virus preparations, nor when a needle dipped in the preparations was scratched across the surface of agar cultures. However, when the first flush of sporophores growing in mushroom trays was inoculated by injecting a small quantity of virus preparation into the base of the young 'buttons' with a hypodermic needle, two out of four trays became infected. Infections at this time (first flush) produced no obvious sporophore abnormalities within the normal cropping period, but the mycelium was infected. This was demonstrated in pure culture by the infectivity tests in Petri dishes, and when mycelium from the two infected trays was added at spawning to trays of healthy mushrooms, abnormal mushrooms appeared and cropping was greatly reduced (figure 6).

Transmission was also obtained in two of three trays when drops of purified virus preparations were applied to the cut surfaces of expanding sporophores. Although relatively successful, these methods are crude, and better ones are being sought. Direct injection of virus into hyphae requires special techniques to avoid the death of the punctured cell and its isolation from its neighbours [11].

Examination for virus particles

Particles characteristic of many plant viruses are visible when virus preparations are stained with potassium phosphotungstate before electron-microscope examination. This, however, gives particle sizes that are slightly smaller than those obtained with mounts that have been shadowed at an angle with a vapourized heavy metal, such as platinum.

Mushroom material collected from one field outbreak of disease gave preparations containing a few 'spherical' particles, approximately 25 mμ in diameter; later preparations, made under more favourable conditions from our routine supply of diseased sporophores, contained a few particles of this kind, and also very many larger 'spherical' particles, about 29 mμ in diameter, and many elongated particles with rounded ends, about 50 mμ long and 19 mμ wide (figure 9).

The larger spherical particles appeared angular, usually hexagonal, in outline, and resembled some of the soil-borne ringspot viruses of flowering plants. The elongated particles are most unusual: the only other plant virus at present known to have this type of particle is lucerne mosaic [5].

For some time, virus particles were found only in the material from intentionally inoculated mushroom trays; the comparable uninoculated control trays produced healthy sporophores in which we could find no evidence of virus. Subsequently, however, the infection spread within the mushroom house. Preparations from apparently symptomless sporophores in one of the uninoculated trays contained the 29 mμ particles, and gave all the other reactions for virus (figure 10). It thus seemed that only one of the viruses had been transferred. Later work has shown that, despite rigorous precautions to prevent contamination during handling, all three types of virus particle can spread from tray to tray within the mushroom house.

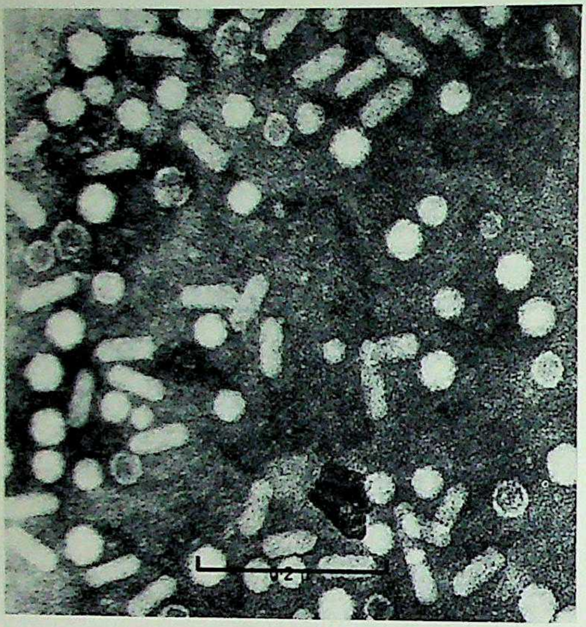


Figure 9 Electron microgram showing virus particles 25 mμ and 29 mμ diameter, and 19×50 mμ.

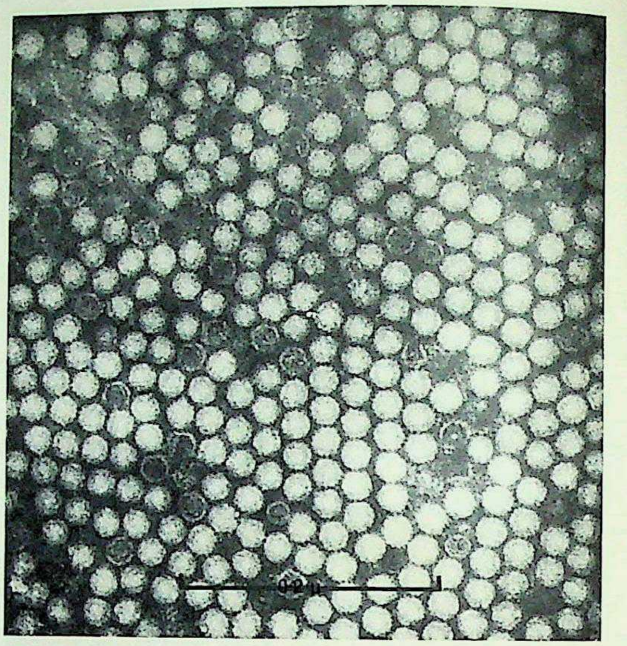


Figure 10 Electron microgram of mushroom virus particles, 29 mμ diameter.

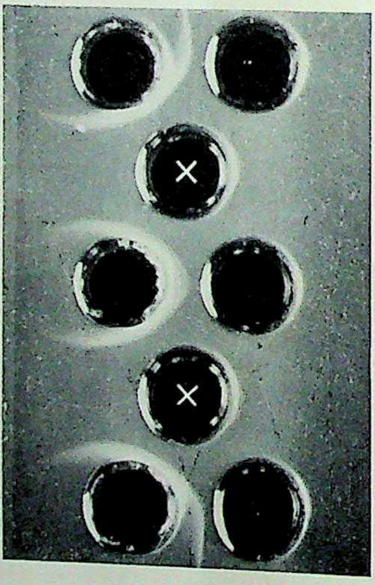


Figure 11 Specific serological reactions in gel-diffusion slide test: three left-hand wells contain purified preparation from virus-infected mushroom; three right-hand wells contain comparable preparations from healthy ones; central wells (X) contain virus antiserum.

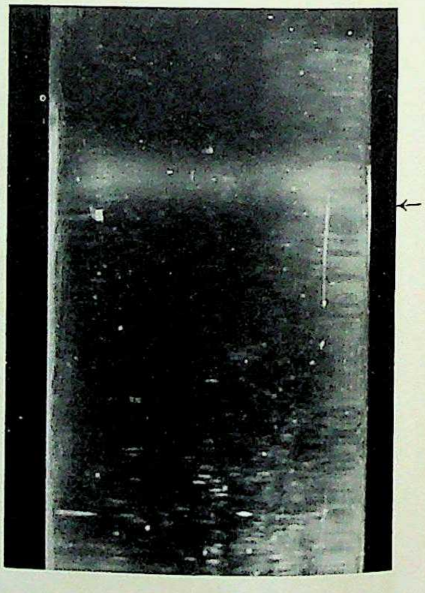


Figure 12 (right) Specific virus zone produced in density-gradient centrifugation.

Serological activity

Proteins and certain other substances injected into animals induce the formation of antibodies. These can be used in specific tests to identify the injected substance. Some plant viruses produce antibodies when injected into rabbits, and the antisera produced are used in identification tests. One of these, the gel diffusion test, is very convenient as it is simple to prepare. It needs only a microscope slide, on which is poured a thin layer of melted Ionagar solution. Several wells are cut out, and the sera and antigen preparations placed in adjacent wells, from which they diffuse outwards. A line of precipitation, clearly visible by simple dark-ground illumination, forms where an antigen and its specific antibody meet in the correct ratio (figure 11).

Our early virus preparations contained much highly antigenic mushroom material. As this was present in both healthy and diseased mushrooms, any reaction involving viruses was obscured. Later preparations, especially those made from young sporophores, contained very little of these host substances, and were used to immunize rabbits by intramuscular injection. The sera obtained reacted specifically with preparations from diseased, but not from healthy, mushrooms. The material injected into the rabbits had contained all three kinds of virus particles, but when the serum was tested against such preparations, only a single reaction line developed in double-diffusion tests. Mushroom virus preparations containing only the 29 mμ 'spherical' particles reacted with the antiserum as well as did preparations containing all three types of virus particles. Whether the 25 mμ spherical particles and the large bacilliform particles are antigenic or not is still uncertain.

Density-gradient centrifugation

If solutions of sucrose containing 100, 200, 300, 400, and 500 g per litre are carefully put in layers in transparent centrifuge tubes, with the most concentrated solution at the bottom of each tube, and then stood overnight, the sharp boundaries between the layers diffuse to produce an even gradient. When a small amount of purified virus preparation is floated on the top of such gradient columns and the tubes centrifuged at high speed, particles in the preparation sediment through the liquid column, eventually reaching levels with densities similar to their own. The levels can be seen as light-scattering bands or zones when the tubes are suitably illuminated from above, and their positions and form are often characteristic for a virus or group of viruses. The more highly purified the virus preparation that is used, the more distinct are the visible zones, for some plant constituents produce light-scattering zones that may obscure any virus zones present. This technique is widely used in plant-virus work, and many of the plant viruses tested in this laboratory give characteristic bluish zones. Preparations made by some methods still contain sufficient of the normal plant constituents, such as ribosomes, to give visible zones, but these zones are typically grey or yellowish-grey in colour, and located above the level of the virus zones. With our early purification method using phosphate buffer extraction, both diseased and healthy mushroom preparations contained copious amounts of mushroom material; this gave a broad, creamy-white upper zone and a broad, grey, diffuse lower band. The non-specific antigens present in extracts from both healthy and diseased mushrooms were confined to the top zone. Borate buffer preparations, however, containing few or no detectable mushroom antigens, did not give these non-specific zones in density gradients, but those from diseased mushrooms produced characteristic bluish zones not found in preparations from healthy mushrooms. After 30 minutes centrifugation, one, sometimes two, specific zones were visible at characteristic levels in the tubes (figure 12). These zones were extracted by a hypodermic needle carefully inserted through the wall of the tube whilst the latter was strongly illuminated. Both zones contained 29 mμ and 19 × 50 mμ virus particles and reacted specifically in serological tests. Comparable samples taken from the gradients of preparations from healthy mushrooms contained no virus particles and did not react with the specific antiserum.

The occurrence of both the 29 mμ and the 19 × 50 mμ virus particles in the same zone is not unexpected, for their calculated volumes are similar. But the reason for there being two zones on some occasions is less readily explained, especially in the preparation containing only the 29 mμ spheres.

Characteristic ultraviolet spectrum

Preparations of those plant viruses that have been adequately purified show a characteristic ultraviolet absorption spectrum. The maximum absorption is in the 260 mμ waveband. Preparations containing only the 29 mμ virus showed this, and the ultraviolet absorption spectrum was closely similar to those of tomato bushy stunt and tobacco mosaic viruses (figure 13).

Other similar diseases

The multiplicity of names (La France, Mummy, Brown, infectious Watery Stipe, and X-disease) reflects the emphasis laid in the original descriptions on particular sporophore abnormalities. Many of these symptoms have been reproduced by our viruses, and our data indicate that the actual signs shown depend greatly upon the growing conditions. Thus, in observing a single disease isolate, watery stipes tended to occur in humid conditions, and dry leathery mushrooms in drier conditions. Throughout, the consistent features have been the degeneration of the mycelium in the compost, and progressive reduction in cropping area, together with abnormal growth in agar cultures We therefore named the disease 'die-back'; it may be that the other disorders of the La France group are also virus diseases, allied to die-back.

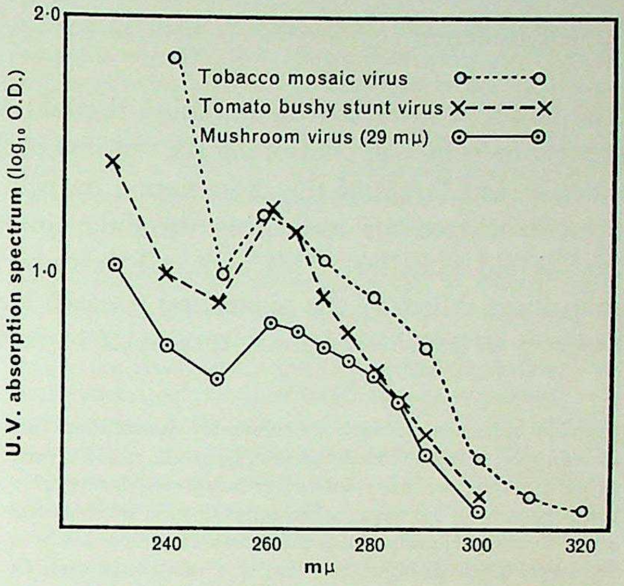


Figure 13 Ultraviolet absorption spectra of purified preparations of tobacco mosaic virus (TMV), tomato bushy stunt (TBSV), and the mushroom virus with particles of 29 mμ diameter.

We have inferred that the particles seen in electron micrograms represent three different kinds of virus, because the 25 and 29 mμ particles have each been found alone, and the 19 × 50 mμ particles are of distinctive shape; but the possibility cannot be excluded that the 25 mμ particles are breakdown products of the larger spheres, reflecting the state of the infected material or the method used in purification. For the task of separating the three viruses we lack the equivalent of the differential hosts used by the plant virus worker; a search for such hosts may be profitable, and might also reveal unsuspected sources of mushroom viruses in unrelated fungi, such as toadstools. Natural spread of all three viruses occurs, but the means is unknown. It seems unlikely, however, that virus is introduced in the spawn, because infected mycelium fails to survive in natural competition in compost. Infection can be carried over from one crop to the next on contaminated trays, although the normal practice of 'peak heating' composts at 55°C for several hours minimizes this. A rational system of control must depend on a greater knowledge of the means of transmission.

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Surface forces in thin liquid films

J. A. Kitchener

The forces of attraction or repulsion that act between particles in colloidal suspensions are of great importance in controlling the stability of the suspension. They are too small to be measured directly, but forces of the same nature operate in thin liquid layers. Ingenious techniques have been developed for measuring the forces in thin liquid layers on solids and liquids, and in free liquid lamellae. This approach has provided a basis for explaining the stability of black soap films. Much of the pioneering research has been done in the Soviet Union and Bulgaria; it deserves to be widely known because of its far-reaching significance in technology and biology.

Colloidal solutions, or 'sols', are commonly classified into two broad types, lyophilic and lyophobic. Lyophilic colloids, such as gum arabic, are macromolecular substances that dissolve spontaneously in an appropriate solvent; their solutions are often viscous and faintly opalescent because the solute molecules are large. Their stability, like that of a solution of sugar in water, is clearly due to solvation. Lyophobic sols, on the other hand, are artificial dispersions of insoluble particles, and they are generally in a delicate state of balance that is easily upset by electrolytes.

The major problem that has always faced colloid chemists is to understand why certain sols are relatively stable while others undergo more or less rapid coagulation; this is a process in which the dispersed particles gather into visible clusters which then settle out of suspension. The stability of sols is of great practical importance in such diverse fields as the formulation of paints and emulsions, the fertility of soils, the filtration of mineral suspensions, and the clarification of waters. It is also involved in many biological problems.

Although Brownian movement has an important effect on sols, it is clearly not the factor that determines stability, as it operates equally in stable or coagulating dispersions. The distinction must lie in the nature of the interactions between the dispersed particles themselves; it seems that in some media the particles attract one another, while in others they repel. Our problem is therefore to investigate forces between very small particles ($< 10^{-4}$ cm in diameter) immersed in liquids. It clearly cannot be done by direct measurement. It has to be approached by combining studies of overall properties of sols—such as electrophoretic properties, and the effects of electrolytes on the stability—with direct experiments on surface forces, carried out on macroscopic bodies. The particular surface force that causes colloidal particles to repel one another, or causes water to form a multimolecular wetting film on clean glass acts normally to the surface. It has been called a 'disjoining force' by B. V. Derjaguin, who has carried out much of the pioneering work in attempting to measure such forces directly.

The present article is mainly concerned with this approach, but it is worth pointing out that the general nature of the colloid forces was first deduced from indirect evidence. By about 1938 it was becoming clear that at least three major types of interaction are concerned, namely:

1. The van der Waals forces of attraction (which, theoretically, exist between all small particles).
2. The electrical forces arising from overlapping of electrical double layers in the liquid around the particles, causing repulsion between particles of like sign, attraction between those of opposite sign.
3. The forces of repulsion arising from solvation of any lyophilic chemical groups on the surfaces of the particles.

During the Second World War, the modern quantitative theory of stability of lyophobic colloids was worked out independently in the Soviet Union by B. V. Derjaguin and L. Landau and in the Netherlands by E. J. W. Verwey and J. Th. G. Overbeek. Leaving aside the still mysterious forces of type 3 (which are primarily important in lyophilic colloids and 'protected' lyophobic colloids), the theory deals with the interplay of forces of type 1 and type 2. It has been, in fact, remarkably successful in giving a consistent interpretation of a wide range of experimental observations. Unfortunately, certain of the fundamental parameters required in the theory can at best be calculated only very approximately. This is one reason why direct measurements of surface forces are needed at the present time. The other is that the old theory of solvation shells, although temporarily out of fashion, has been shelved only for lack of theoretical understanding of solvation. Its viability is amply proved by the existence of non-ionic detergents. As there seems little hope of developing a mathematical theory of solvation at the present time, an empirical approach to this problem also is urgently needed.

Surprisingly, it is some recent experiments on very thin liquid lamellae that have begun to yield information on all three types of colloid force. The more obvious approach of directly investigating forces between pairs of solid bodies—or one half of that system, a single solid body and its liquid wetting film—has also been explored in a number of pioneering experiments. This work by Derjaguin and his co-workers in Moscow has produced some interesting results, though the difficulties of such experiments with solids are very great.

Derjaguin showed that the forces of interaction between bodies of various shape could be calculated from a knowledge of the disjoining pressure per cm^2 for a pair of flat plates as a function of the thickness of the liquid film between them. The concept of disjoining pressure represents the fact that the energy of an interfacial system depends on the dimensions of the phases as well as on their interfacial areas. In principle, this has long been recognized; for example, with sufficiently small drops the surface tension of a drop must change with radius. But the problem is the range of action and magnitude of these effects, and even their sign, for negative disjoining pressures are found in some thin films. Various thermodynamic consequences of the phenomenon have been deduced by Derjaguin—for example, the possible adsorption isotherms for a vapour near saturation; the effect of radius on the angle of contact of small drops; the incidence of 'dropwise condensation'

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of vapours; and the interpretation of capillary condensation data for porous adsorbents.

The number of actual measurements of disjoining pressures, however, is still small. Both the experimental aspects and the theoretical interpretation of the effects pose problems of great interest at the present time.

Experiments on the range of action of surface forces.

The solid/liquid interface. A simple qualitative experiment, originally due to the Hungarian colloid chemist von Buzagh, demonstrates the existence of forces of repulsion between silica surfaces in water. Microscopic (1–5μ) particles of quartz are allowed to settle from pure aqueous suspension on to a silica microscope-slide and are then examined carefully under high magnification. They are seen to be undergoing slight lateral Brownian motion, showing that they are not in actual contact with the slide. If, however, a sufficient amount of a suitable electrolyte (such as would flocculate a silica sol) is added, the motion ceases. This is because the particles are no longer repelled from the plate. The disjoining force concerned here is of the order of 10^{-8} dyne, and the range of action is probably sub-microscopic.

As early as 1936 Derjaguin (with Obuchov) attempted to measure the repulsive forces between cleaved sheets of mica of 1 cm^2 area under liquids. Significant differences were found with polar and non-polar liquids, but the magnitude of the disjoining pressures recorded now seems much too high. So, too, does the range of action, *c.* 1μ, deduced from interference colours. This seems a fantastically difficult experiment to hope to carry out successfully, as the two solids have to be smooth, flat, and parallel, all to within much less than a micron, as well as completely free from dust. Nevertheless, in 1953 Derjaguin and Abricosova [1] succeeded in measuring long-range van der Waals forces directly *in vacuo* and their results were later confirmed in London [2] and Utrecht [3]. Measurement of disjoining pressures in liquids is even more difficult. Indeed, it is only quite recently that Derjaguin succeeded in measuring the force barrier opposing contact between two solids in a liquid [4]. This was done with two thin, crossed, platinum wires, and even so it was not possible to determine the distance between the wires at which the force operated. The disjoining pressure isotherm ($P=P(h)$) could therefore not be deduced. No force barrier could be detected with non-polar liquids such as carbon tetrachloride; with aqueous electrolytes the barrier changed in the expected manner with the electrical potential applied to the wires. It was at a minimum near the point of zero charge.

The thinning of wetting films on solids. In 1939, B. V. Derjaguin and M. M. Kusakov [5] carried out an ingenious experiment to see if a liquid formed a stable multimolecular film on a solid. A small bubble of gas was pressed against a sheet of freshly cleaved mica or freshly blown glass under a liquid, and the thinning of the intervening liquid film was noted by observing the Newton's rings under a microscope. With water, plane multimolecular films remained on the solid. Their thickness (0·1–0·3μ) depended on the pressure inside the bubble. With alcohol, no stable films of measurable thickness were obtained. Unfortunately, this crucial experiment has never been adequately confirmed. When G. A. H. Elton [6], and L. F. Evans [7] repeated the experiment they did not obtain equilibrium films on glass, although Evans did observe them on silver in very dilute solutions of a wetting agent. It is clear that all experiments of this type, in which small single bubbles are kept for many minutes in pure water or solutions of inorganic compounds, are excessively susceptible to contamination by infinitesimal traces of surface-active impurities. These are extraordinarily difficult to remove from water and from the surfaces of solids, and their presence may explain the discrepancies.

Evans was more concerned with the mode of contact of a bubble with a solid that had deliberately been rendered hydrophobic. He used surface-active substances of the class used as 'collectors' in the froth-flotation of minerals—for example, cetyl trimethylammonium bromide, a collector for quartz. He found that as soon as a ring of thinned liquid developed, the bubble almost instantly made contact with the solid, and the wetting film ruptured. High-speed cinephotography has shown that contact between rising bubbles and small mineral grains in practical flotation occurs within about 0·001–0·01 sec if the mineral has been rendered strongly hydrophobic. The degree of hydrophilic or hydrophobic character is generally judged by the angle of contact at the air-liquid-solid boundary. Feebly hydrophobic grains are not collected by rising bubbles, but, according to Russian workers, contact can be brought about in a static system by pressing the grains against the bubble for longer periods.

Such observations suggest that the same factors are involved in the thinning of wetting films on solids as in the stability of colloidal dispersions. At one extreme are the strongly hydrophilic surfaces on which thinning of the wetting film is opposed by a positive disjoining pressure, and at the other are strongly hydrophobic surfaces where a negative disjoining pressure develops at a certain critical film thickness. In intermediate cases there may exist a small potential energy barrier, which, once surmounted, is followed by a region of instability. These classes correspond in colloids to stable dispersion, rapid coagulation, and slow coagulation, respectively.

A liquid may spontaneously recede from a solid surface as in the 'dropwise' condensation of steam on copper condenser-tubes treated with montan wax. This system is one, according to A. N. Frumkin, in which wetting films of certain thicknesses are unstable and break down into discrete droplets. These are separated by areas carrying invisible adsorption layers that may be either monomolecular or multimolecular. Derjaguin has emphasized that such adsorption layers may have a structure different from that of the bulk liquid. This follows also from the fact that although they are at the same chemical potential—being in equilibrium—they have different partial molar heat contents. This is because adsorption is accompanied by a net evolution of heat and consequently layer and liquid have different partial molar entropies.

This line of thought suggests another possible method of investigating disjoining pressures in thin wetting films—namely, by studying the influence of film thickness on vapour pressure. Normally, with macroscopic quantities of liquid, vapour pressure (p_0) is independent of thickness (h); but where surface forces introduce a positive disjoining pressure, P, evaporation of the liquid is resisted and the vapour pressure is reduced according to the thermodynamic equation

$$PV=\boldsymbol{R}T\ln p_0/p_h$$

(in which p_h is the vapour pressure of the film, V is the molar volume of the liquid, $\boldsymbol{R}$ the gas constant, and T the absolute temperature). To determine P as a function of h, therefore, one can investigate the amount of adsorption from the vapour state at controlled partial pressures very close to saturation.

This exacting experiment was successfully performed by B. V. Derjaguin and Z. M. Zorin [8]. The solid substrate consisted of an optically flat glass plate (figure 1). The relative saturation, p/p_0, of vapour was controlled by maintaining a

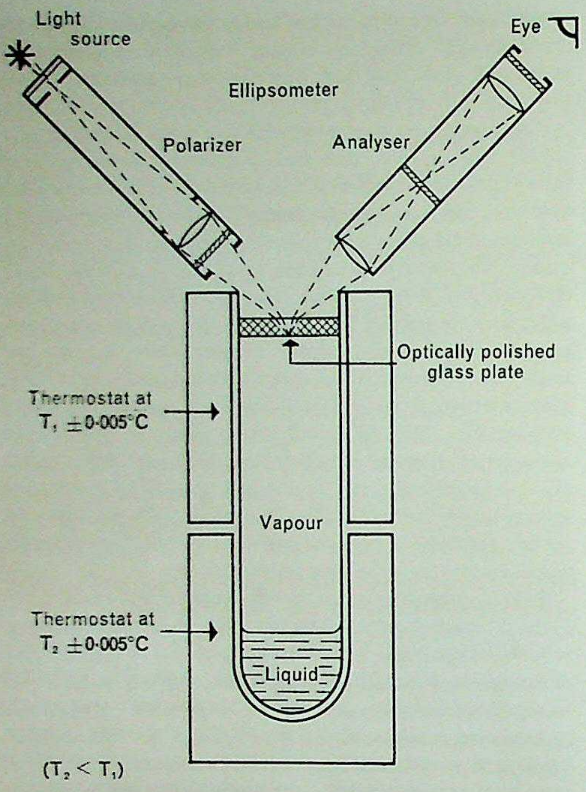
Light source
Eye
Ellipsometer
Polarizer
Analyser
Optically polished glass plate
Thermostat at $T_1 \pm 0{\cdot}005$°C
Vapour
Thermostat at $T_2 \pm 0{\cdot}005$°C
Liquid
$(T_2 < T_1)$

Figure 1 Schematic diagram of the method of Derjaguin and Zorin for determining the thickness of adsorption layers on glass [8].

small temperature difference between the plate and a reservoir of pure liquid, and the thickness of the adsorbed film was determined by means of an ellipsometer. This is a polarizing microscope with which the degree of elliptical polarization of the light reflected at an oblique angle from the glass surface can be analysed. The method is very sensitive (±5Å), provided that the refractive index of the layer is known or can be assumed.

The results obtained by Derjaguin and Zorin with a number of liquids on glass are remarkable. Multimolecular adsorption layers were always obtained if p/p_0 was between 0·95 and 1·0. However, there was a striking difference between non-polar liquids and polar liquids. The former increased in thickness continuously as p approached p_0, and the films eventually showed interference bands. With the polar liquids, the isotherm intersected the ordinate at a definite limiting thickness—for example, 60 Å with ethanol—and any further condensation appeared as micro-lenses of dew, with no change in the thickness of the areas on the plate between the lenses. These observations demonstrate the existence of positive disjoining pressures in wetting films. By inference, the non-formation of thicker films in certain cases indicates negative disjoining pressures for such hypothetical films. Derjaguin considers that the discontinuity of properties with multilayers of polar liquids arises from a phase difference induced by orientation in the adsorption layer. Some confirmation of this orientation is given by other experiments in which he found that such layers, especially in oils, have abnormally high viscosity. A slightly odd feature of the results was that polished glass behaved as a hydrophobic substrate and formed a limiting layer 17 Å thick with water. It is usually considered to form zero angle of contact; contamination may be the cause of this result.

Liquid films on other liquids. There is a similarity between the observations described above for liquid films on solids and the spreading characteristics of liquids on other immiscible liquids. Non-polar liquids such as benzene do not form stable multimolecular films on water. The initial spreading is followed by retraction as the film breaks into micro-lenses floating on a substrate that carries a monomolecular adsorption layer. This phenomenon is usually interpreted in terms of surface tension. For example, in the benzene–water system, the surface tension of benzene against air is 29 dyne cm^{-1}, the interfacial tension benzene–water is 35 dyne cm^{-1}, and the surface tension of water saturated with benzene is 62 dyne cm^{-1}. As $(29+35) > 62$, a droplet contracts into lens form rather than spreading to a duplex layer. This interpretation, although formally correct, passes over the interesting question why a monolayer is more stable in this system than, say, a bimolecular or multimolecular layer. It must mean that the surface tension of water carrying a multilayer of benzene is greater than 62 and less than 64 dyne cm^{-1}. In other words, the surface free energy of adsorption layers of benzene on water increases with thickness of layer; this is equivalent to a negative disjoining pressure in the multilayers.

The spreading of one liquid on another offers some experimental advantages compared with the liquid–solid system. The most notable are the smoothness of the surfaces and the easier control of contamination. Most experiments have been performed with water as the substrate, because its surface tension is higher than that of most other liquids. All other liquids, whether polar or non-polar or mixtures, behave in the same way as does benzene. It seems that thick multilayers of organic liquids are generally unstable. Even the familiar coloured rings formed by oil patches on wet roads are transient non-equilibrium systems that, in time, break up into an invisible monolayer and micro-droplets.

The instability of thick layers of organic liquids reveals a negative disjoining pressure. Positive disjoining pressures might be expected with aqueous electrolytes, but in order to prepare layers of water it is necessary to find a liquid of higher surface tension to spread it on. Mercury is the only convenient one, but it is an extremely difficult substance to purify adequately. Like all metals, it chemisorbs oxygen and other gases instantly on contact with air. The first reliable experiments on the wetting characteristics of mercury were done by A. Frumkin and A. Gorodetskaya in 1938 by the bubble-contact method [9]. They found that wetting films collapsed spontaneously and an angle of contact was established. Mercury is of particular interest because its surface can be polarized at definite potentials, thus establishing a controlled electrical double layer at the mercury–solution interface. Experiment shows that the angle of contact is maximal at the zero point of charge and decreases at more positive or more negative potentials. It also decreases with addition of electrolytes to the aqueous phase. Evidently an electrical double layer in the region between the charged mercury and uncharged air bubble exerts a positive contribution to the disjoining pressure. This layer can partially or wholly offset the inherent instability of the water films on mercury.

The difficulties due to impurities and the reactivity of mercury are least troublesome if a pure hydrocarbon is used as the second liquid. The most accurate and elegant experiments of this kind have been published by A. Scheludko and D. Platikanov [10] for films of benzene on mercury. Their ingenious and refined technique depends on recording automatically the changing thickness of the liquid film at a small area of contact (0·01 mm diameter) between a concave meniscus of benzene and a convex meniscus of mercury (figure 2). A sensitive

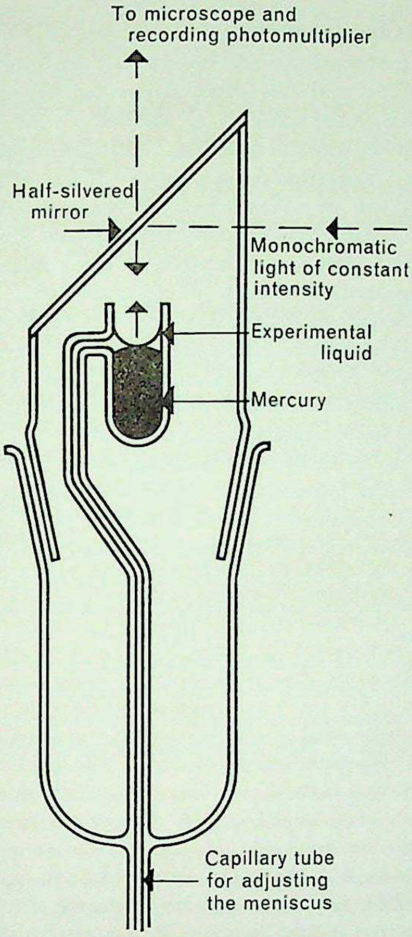
To microscope and recording photomultiplier
Half-silvered mirror
Monochromatic light of constant intensity
Experimental liquid
Mercury
Capillary tube for adjusting the meniscus

Figure 2 Principle of the apparatus used by Scheludko and his co-workers for measuring the reflectivity of microscopic liquid lamellae or films on mercury [10, 13].

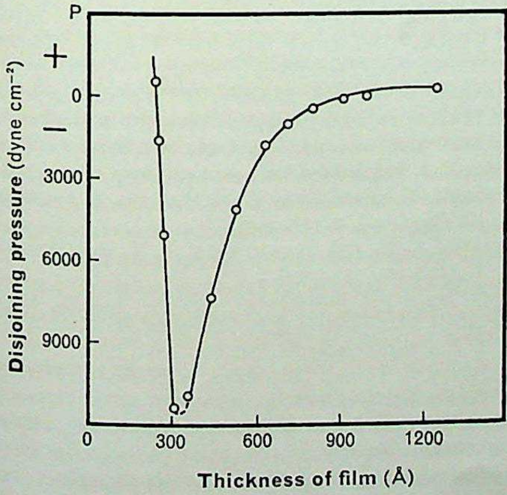

Figure 3 Graph of the 'disjoining pressure' in films of benzene on mercury, as a function of thickness [10].

photo-electric photometer and microscope were used to determine the intensity of light reflected from the area; this gave the film thickness. They assumed that the liquid as a layer retained its normal viscosity and calculated the effective pressure acting on the film from the rate of thinning. As the external capillary pressure was known, the internal disjoining pressure could be obtained by difference as a function of film thickness. The results (figure 3) show that the films between about 240 and 1000 Å in thickness were inherently unstable (P being negative). Theoretical reasons for the complicated form of the $P(h)$ curve were suggested.

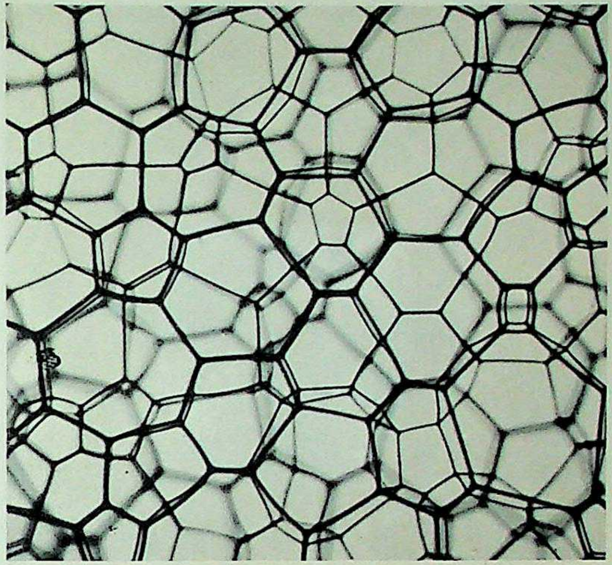

Figure 4 A well-drained soap foam, consisting of polyhedral cells with very thin lamella walls.

It should now be clear why the ideal system for the study of disjoining pressures would be a lamella, a free film of liquid. Such lamellae cannot be prepared with pure liquids as the negative disjoining pressure will continue to thin the film until it ruptures. If a lamella of liquid is to be formed, an element of elasticity must be present, so that further stretching of the already thinned parts of the film is hindered. This is the function of the soap or other surface-active substance in any liquid that yields a foam, and solutions of these substances provide the most favourable conditions for studying disjoining pressures.

Surface forces in foams

There are three types of foam. With viscous pure liquids (such as glycerol) a temporary dispersion of bubbles, a round-bubble foam, can be made, but no lamellae are formed; the bubbles coalesce instantly when the liquid has drained from between them. Secondly, with dilute solutions of non-ionic surface-active compounds (such as octyl alcohol), a transient foam is obtained. Thick planar lamellae are formed at first between bubbles, but they thin down steadily and collapse under the action of van der Waals forces on reaching a critical thickness. Finally, soaps, detergents, and proteins yield a persistent foam that, after draining, consists of polyhedral cells with very thin walls (figure 4).

For centuries the stability—or, strictly, metastability—of soap films has fascinated and baffled the greatest scientists. Robert Boyle, Newton, Gibbs, Rayleigh, Perrin, and many lesser men have puzzled over the fact that when a soap film is allowed to drain undisturbed the beautiful coloured interference bands finally give way abruptly to extremely thin black films that cease to thin any more (figure 5). The problem is the nature of the internal forces that counterbalance the external hydrostatic suction. Classical surface tension and surface viscosity do not provide a satisfactory explanation of black films, and it is only quite recently that the origin of the positive disjoining pressures has been even partially elucidated.

J. F. Goodman and co-workers [11] used radioactive tracers to prove that stable black soap films consist of sandwiches of

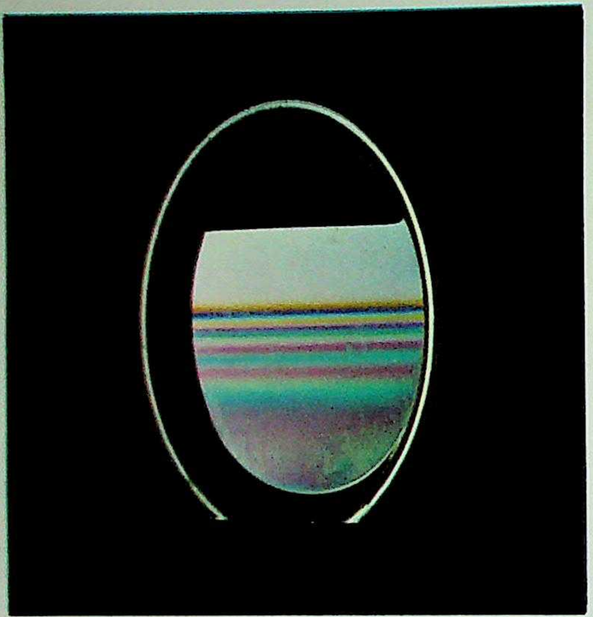

Figure 5 As a coloured soap film drains, the silver-grey band is followed by the uniform black film; at the sharp junction the thickness falls abruptly, e.g. from *c.* 500 Å to *c.* 100 Å.

solution between two monomolecular close-packed adsorbed layers. With ionic detergents, the thickness ranges from about 200 Å in solutions of low ionic strength down to a limiting value of about 55 Å in the presence of much salt; with non-ionic detergents, a low equilibrium thickness, independent of the presence of salts, is obtained. These observation confirm the earlier pioneering work of Derjaguin and Titievskaya [12], who were the first to determine equilibrium thicknesses in horizontal microscopic free films formed by bringing together a pair of bubbles under a solution. They demonstrated the role of electrical double-layer forces in counterbalancing the hydrostatic pressure and the van der Waals pressure. These authors were also the first to point out that, when electrical double layers have been completely swamped, there still remains in the thinnest soap films a positive disjoining pressure of a different nature; it appears to arise from the mechanical strength of the two back-to-back adsorption layers carrying, possibly, a thin sheet of water of hydration attached to their hydrophilic groups.

Most recently, Scheludko's refined microscopic method has been used by Scheludko himself and D. Exerowa [13] in Sofia in a very remarkable series of measurements of the kinetics of thinning and of the equilibrium thickness of free films. By studying a range of thicknesses and different ionic strengths, it has been possible to determine separately the electrostatic component and van der Waals component of the disjoining pressures. As space does not permit doing justice here to Scheludko's outstanding series of investigations, interested readers are referred to a fascinating account that this author has given of his work [14]. It seems certain that Scheludko's elegant technique will soon lead to further information of great value to colloid science.

Theoretical developments

Scheludko confirmed the $1/h^3$ law for van der Waals pressure in liquid films, and this confirmation can be regarded as substantiation of the principle of additivity of intermolecular attraction forces, first developed by London in 1932; the other confirmation comes from the direct measurement of long-range (> 1000 Å) van der Waals forces between polished plates [1–3]. Nevertheless, the London theory is well known to be over-simplified, and it is, therefore, of great interest that a more generalized treatment of electromagnetic attraction between macroscopic bodies has been developed by E. M. Lifshitz [15] and extended to liquid wetting films by I. E. Dzyaloshinskii, E. M. Lifshitz, and L. P. Pitaevskii [16]. A variety of forms of disjoining pressure isotherm are theoretically possible, but unfortunately the necessary data for numerically evaluating the forces by this theory are not available.

The theory of interaction of electrical double layers is also based on an over-simplified model, and the influence of ionic size and of discreteness of charge are now being examined theoretically [17]. However, it is questionable whether the experimental data so far available justify introduction of these refinements.

Finally, as to the stability of solvation sheaths, no theoretical basis exists for estimating their effects in colloidal systems while solvation remains one of the classical unsolved problems of physical chemistry. New experimental data are all the more desirable.

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Ion exchangers

D. Reichenberg

Ion exchangers have been known for over a hundred years, and are familiar in water softeners. However, the forces responsible for the binding of the exchangeable ions have not been clearly understood. This article discusses the nature of ion exchangers, summarizes some recent work on theories of ionic selectivity, and indicates the significance of ion-exchange processes in biological systems.

Ion-exchange materials (or ion-exchangers) are solids that can, as their name implies, exchange the ions present in the material for others in a solution [1]. Their most familiar use is in the domestic water softener, where the soap-precipitating calcium and magnesium ions are removed from hard water and replaced by sodium ions. Water softening is the largest application of ion exchange, but there is a wide range of other applications already in use and others that await exploitation. Exchangers are insoluble acids or bases, which are insoluble because they consist largely of macromolecules, often, though not always, crosslinked to one another. Attached chemically to the network are polar groupings that may ionize into fixed ions, which remain attached to the network, and free mobile counter-ions. The counter-ions can exchange with any ions in a solution in contact with the exchangers.

The ionizable groups are primary in importance, since they actually participate in ion-exchange processes, though the polymeric networks must also be considered as they control the environment in which these processes occur.

Exchange groupings may be described as acidic (cation exchangers) and basic (anion exchangers). Each may be conveniently subdivided into 'strong' and 'weak'. Thus there are four types of grouping, strong acid, weak acid, strong base, and weak base. Within each of these four types, there may be more than one kind of grouping. Thus the following are different kinds of weak base anion-exchange grouping: $—NH_2$, $—N(CH_3)H$ and $—N(CH_3)_2$. A monofunctional exchanger contains only one kind of grouping. A polyfunctional exchanger contains more than one kind of grouping, though the different kinds of grouping present may be of the same type.

Monofunctional exchangers may be divided into the same four types as the groups they may contain, each with its advantages, depending on the application in mind. Their properties are much simpler and more clear-cut than those of polyfunctional exchangers so that they are easier to study and to use. Most present-day knowledge and practical applications are based on monofunctional exchangers. Of these, the best known and most widely used are the ion-exchange resins.

Ion-exchange resins

The nature of the polymeric network of a resin depends on its mode of preparation. Excluding modified natural products such as sulphonated coals, the earliest resins were based on phenol-formaldehyde polycondensations, and on aromatic amine-formaldehyde polycondensations. However, the most important property of the polymeric network is the effective degree of crosslinking, and this was not easy to control by these earlier preparative methods. Modern resins, therefore, are made by addition copolymerization reactions. One of the most useful of these is the copolymerization of styrene with divinylbenzene (DVB). By varying the proportion of divinylbenzene, the effective degree of crosslinking may be readily controlled and varied. The crosslinked polystyrene may be sulphonated directly to give a strong-acid cation exchanger containing nuclear sulphonic acid groups. Alternatively, it may be chloromethylated and the product reacted with an amine to give an anion exchanger, either strong or weak depending on the type of amine used—ammonia and primary and secondary amines give weak base exchangers, while tertiary amines give strong base exchangers. The chloromethylated product may be converted to the nitrile and then hydrolysed to give a weak-acid cation exchanger. Weak-acid cation exchangers can also be prepared by the direct copolymerization of methacrylic acid with divinylbenzene.

For most purposes, the structure and composition of a resin is defined by the nature of the exchange group; by the degree of crosslinking, usually defined by the percentage of crosslinking agent used in the initial copolymerization; and by the specific ion-exchange capacity. This last is defined as the number of milligram equivalents of fixed exchange groupings per gram of dry resin in a given ionic form. For cation exchangers, this is usually the hydrogen form; for anion exchangers it is usually the chloride form. The number of milligram equivalents of fixed groups is, of course, equal to the number of milligram equivalents of counter-ions that can be exchanged.

The most important properties affecting the use of ion-exchangers are swelling, rate of exchange, and exchange selectivity. In the case of ion-exchange resins, all these are markedly affected by the degree of crosslinking. In order to decide on the optimum degree of crosslinking, the main considerations are the swelling and the exchange rate. In nearly all cases, the effective use of ion exchangers depends on their being swollen in a suitable liquid. The ionizable groupings are polar, and therefore ion exchangers swell in water, aqueous solutions, and other polar liquids (figure 1). The higher the crosslinking, the lower the degree of swelling. A resin of low crosslinking therefore occupies, when swollen, a greater bed-volume for a given ion-exchange capacity and so is uneconomical of space. In addition, resins swollen in water shrink in electrolyte solutions and the effect is more marked with resins of low crosslinking (figure 2). Such changes of volume tend to disturb the uniform packing of resin columns. As it is usual to work with resin columns and with solutions of different concentrations, the regenerant solution being normally much more concentrated than the exhausting solution, one is often limited to resins of medium and high crosslinking. However, the rates of ion-exchange should be as high as possible, particularly for chromatography. These rates decrease with increase of crosslinking (figure 3). One is therefore often forced to a compromise between the conflicting demands of low swelling, which requires a high crosslinking, and a high exchange rate, which requires low crosslinking.

The most usual commercial strong-acid cation exchange

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Was born in London in 1921 and educated at the University of London. He started research at the Laboratory of Colloid Science, Cambridge, and after war service and further research at Queen Mary College, London, joined the Chemical Research Laboratory (later renamed the National Chemical Laboratory), Teddington, in 1948. His research interests, in addition to the phenomena associated with ion exchangers, include the selective uptake and accumulation of ions by biological systems.

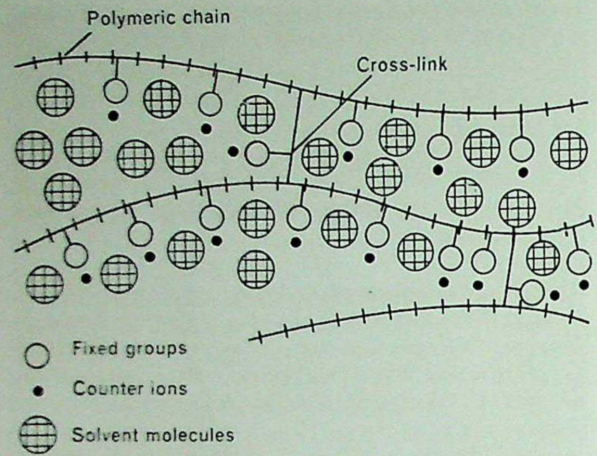

Figure 1 Diagrammatic representation of the interior of an ion exchanger.

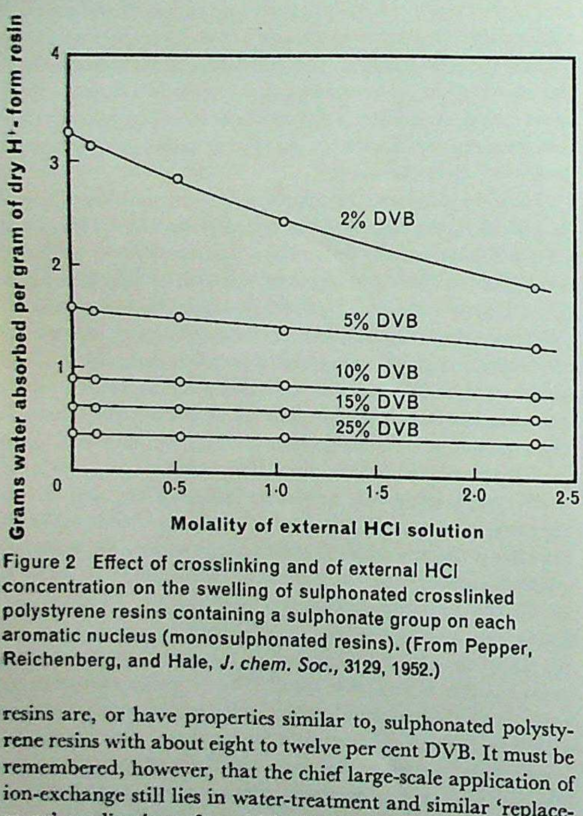

Figure 2 Effect of crosslinking and of external HCl concentration on the swelling of sulphonated crosslinked polystyrene resins containing a sulphonate group on each aromatic nucleus (monosulphonated resins). (From Pepper, Reichenberg, and Hale, *J. chem. Soc.*, 3129, 1952.)

resins are, or have properties similar to, sulphonated polystyrene resins with about eight to twelve per cent DVB. It must be remembered, however, that the chief large-scale application of ion-exchange still lies in water-treatment and similar 'replacement' applications, for which this kind of resin was mainly developed. Where simple inorganic ions are being replaced, eight to twelve per cent DVB is satisfactory. However, organic ions exchange more slowly than simple inorganic ions. Hence for the exchange of organic ions, particularly in chromatography, a lower degree of crosslinking is desirable. Similar remarks apply to the shape and size of the resin particles. They are usually made in the form of spherical beads (figure 4), a form well suited to column techniques. The exchange rate decreases with increasing particle size, and, while particle diameters of 0·3 to 1·5 mm are suitable for replacement techniques, smaller beads (0·05 to 0·2 mm) are preferable for chromatography. Many resins are now commercially available with degrees of crosslinking from 1 to 20 per cent DVB and with particle diameters from 0·05 to 1·5 mm. Where resins with a sufficiently small particle size are not available, the exchange rate may be increased by raising the temperature. This possibility may be limited by the chemical stability of the material being processed and of the resin, particularly in the case of anion exchangers. Cation-exchange resins may be safely heated to 120°C and even a little higher; anion-exchange resins are, in general, less stable and should not be heated above about 60°C.

Ion exchangers are most frequently used in aqueous media. However mixed aqueous-organic or even purely organic media may be used, provided they swell the exchanger satisfactorily.

It has been mentioned that large organic cations exchange slowly with resins of medium or high crosslinking. This is normally a disadvantage, but may be sometimes exploited to separate small ions from large ones. This is commonly known as the 'sieve effect'.

It is difficult for very large organic ions or molecules to diffuse through the 'pores' of conventional resins. To overcome this, 'macroreticular' resins have recently been developed [9]. These have wide 'channels' (400 Å to 10 000 Å) penetrating the resin particles (figure 8). Such resins should be useful in replacement techniques (for example sugar refining), ion exchange chromatography, solubilization chromatography, and in applications involving 'ion-exclusion', ligand exchange, and catalysis.

Ionic selectivity

Relative affinity or ionic selectivity is the ability of an exchanger to discriminate between different counter-ions. It is markedly affected by the degree of crosslinking. Resins of very low crosslinking, for example 1 per cent DVB, have very little selectivity. This does not matter much with replacement techniques but is of importance in the case of chromatographic separations, as these depend primarily on affinity differences.

Relative affinity may be defined quantitatively as follows. Consider an exchanger and its equilibrium with two monovalent counter-ions, A and B, present both in the exchanger and in the solution in contact with it. We may write:

$$\bar{A} + B \rightleftharpoons A + \bar{B} \qquad (1)$$

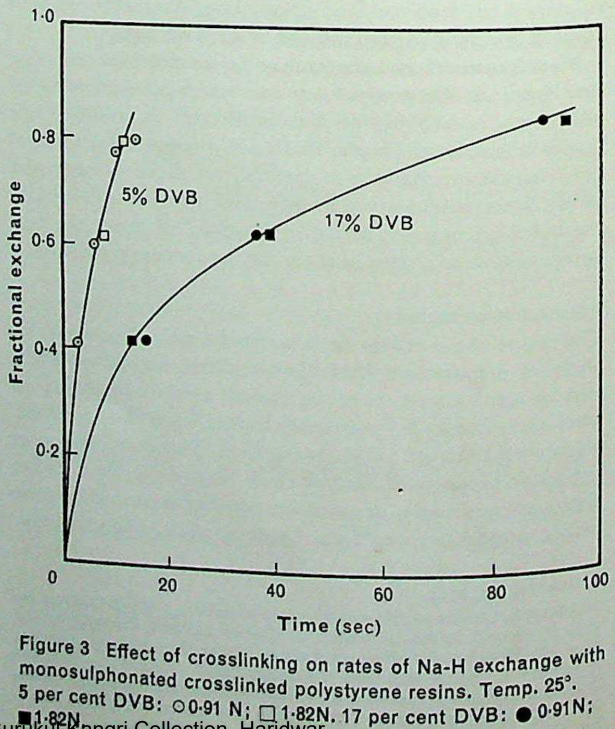

Figure 3 Effect of crosslinking on rates of Na-H exchange with monosulphonated crosslinked polystyrene resins. Temp. 25°. 5 per cent DVB: ○ 0·91 N; □ 1·82N. 17 per cent DVB: ● 0·91N; ■ 1·82N.

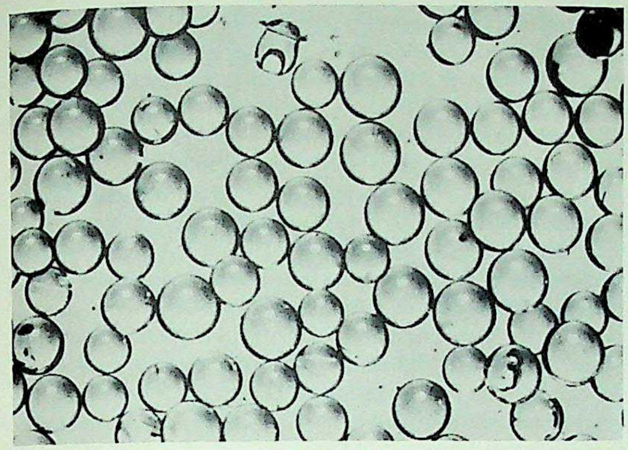

Figure 4 Resin beads [9]. (×10 approx.)

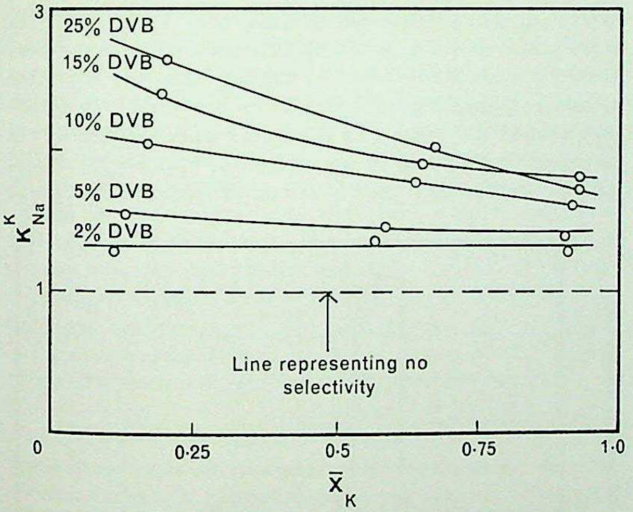

Figure 5 Effect of crosslinking and of ionic composition on selectivities in the potassium-sodium system with monosulphonated crosslinked polystyrene resins. (From Reichenberg and McCauley, *J. chem. Soc.*, 2741, 1955.)

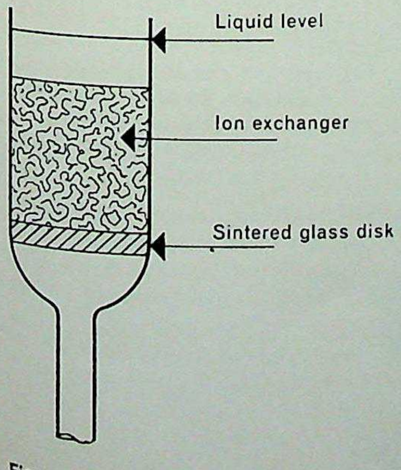

Figure 6 Simple ion-exchange column

the bars indicating the resin phase. Then the selectivity coefficient (or relative affinity coefficient) is defined by:

$$K_A^B = \frac{\bar{X}_B}{\bar{X}_A} \cdot \frac{a_A}{a_B} \tag{2}$$

where X represents equivalent fractions of the counter-ion on the exchanger ($\bar{X}_A + \bar{X}_B = 1$) and a the activities of the ions in solution. In general, K_A^B varies with varying ionic composition (figure 5), but for monovalent counter-ions and a given ionic composition, that is with $\bar{X}_A$ or $\bar{X}_B$ constant, K_A^B hardly varies at all with change in the total concentration of the solution. Thus with monovalent ions and a given activity ratio a_A/a_B, the ionic composition of the resin will be almost unaffected by the degree of dilution of the solution. The reverse is the case with heterovalent exchange, when the two counter-ions A and B have charges of different magnitude. Here equations (1) and (2) are inapplicable.

Consider the case of the ions Na^+ and Ca^{++}. We must now write

$$Ca^{++} + 2\overline{Na^+} \rightleftharpoons \overline{Ca^{++}} + 2Na^+ \tag{3}$$

and therefore $$K_{Na^+}^{Ca^{++}} = \frac{\bar{X}_{Ca^{++}}}{(\bar{X}_{Na^+})^2} \cdot \frac{(a_{Na^+})^2}{a_{Ca^{++}}} \tag{4}$$

There is some doubt as to whether $X_{Ca^{++}}$ and X_{Na^+} should be defined as the equivalent or the mole fractions of the ions on the exchanger. However, in either case, it may readily be shown that the relative amounts of Ca^{++} and Na^+ on the exchanger now depend on the total concentration of Ca^{++} and Na^+ in the solution. It may be shown from equation (4) that in heterovalent exchange, for a given concentration ratio of the counter-ions in solution, increasing dilution of the solution favours the uptake by the exchanger of the counter-ion of higher valency. This has been confirmed experimentally. The effect, which is known as the 'concentration-valency' effect, increases with the difference in valency of the two ions involved. It is of considerable importance in a number of practical ion-exchange applications. In water softening, for example, calcium and magnesium ions are readily removed from tap water in exchange for sodium ions, since the tap water is a dilute solution. In regenerating the exchanger, a concentrated sodium chloride solution is used and the calcium and magnesium are stripped fairly readily from the exchanger.

When it is desired to displace an ion A from an exchanger and replace it to more than 99 per cent by an ion B, it is necessary for the ratio a_B/a_A to exceed $100/K_A^B$. This would often involve inconveniently high concentrations of B in solution. The problem may be solved nearly always by the well-known method of removing the products of reaction as they are formed. This is readily achieved by running the solutions through a column of the exchanger in a filter-tube (figure 6). The use of such ion-exchange columns is standard practice in nearly all ion-exchange work, especially ion-exchange chromatography. However, the use of columns does not avoid the necessity for alkaline solutions when converting weak acid exchangers from the hydrogen form to other ionic forms, or for acid solutions when converting weak base exchangers from the free base form to other forms.

Complexing

The use of reagents that form complexes with one of the products of a reaction to drive the reaction to completion is, of course, familiar. In a similar way, one may use, in the eluant solution, an agent that complexes in solution with the ion to elute that ion efficiently from an exchanger. The most obvious example is the use of the hydroxyl ion to 'elute' hydrogen ions from a weak-acid cation exchanger (see above). The anions of weak acids will serve for this purpose also, although not as effectively as the hydroxyl ion. Where the counter-ion to be taken up or removed from the exchanger is the anion or cation of a weak acid or base, any means of altering or controlling the pH of the solution can be used to influence the exchange behaviour. Thus in cases where differences of affinity of the counter-ions for the exchanger are insufficient in themselves to achieve a satisfactory separation, one may exploit differences in their 'solution chemistry' to achieve this separation. An example of this is the use of complexing agents such as citric acid to improve the separation of rare-earth ions.

In connection with complexing, it is appropriate to mention that ion exchange has been used extensively for the detection, identification, and sometimes separation of a number of complex ions, previously unknown or not well established. In particular, K. A. Kraus and F. Nelson [4] have shown that in very concentrated solutions ($> 5N$) of hydrochloric and hydrofluoric acids, a number of metals form complex anions that have an extremely high affinity for anion exchangers. On dilution of the acid with water, the complexes break up, and are readily stripped from the exchanger. In many cases, separations can be achieved by control of the acid concentration, as each complex breaks up at its own characteristic acid concentration.

Applications to non-ionic substances

Ion-exchange techniques in themselves can be applied only to ions. However, in certain favourable circumstances, substances which are by themselves completely non-ionic may be complexed with certain simple ions to form 'compound' ions. Thus some polyhydroxy compounds can be combined with borate ions, and aldehydes and ketones with bisulphite ions. The usual ion-exchange techniques may now be applied to these complex ions. Various sugars, aldehydes, or ketones for example, may be separated from one another by ion-exchange chromatography [20].

Analogous to this in some ways is a new technique, 'ligand exchange', recently developed by F. Helfferich [2] on the basis of earlier observations by R. H. Stokes and H. F. Walton [3]. Here a suitable metal cation is absorbed on to a suitable ion exchanger, and the unsatisfied coordination valencies of the metal ion are used for the absorption of ligand molecules. Provided the attachment of the metal ions to the fixed groups of the exchanger is sufficiently strong, various ligands can be exchanged for one another without any removal of the metal ions from the exchanger occurring. In this way, ligands can be separated from non-ligands or from one another, owing to their different strengths of attachment to the metal ion.

Applications not dependent on ion exchange

The foregoing is a brief account of ion-exchange phenomena in relation to their possible applications. However, there are a number of other phenomena associated with ion exchangers that can be exploited to practical ends. Electrolytes are absorbed to a relatively small extent into the interior of ion exchangers, whereas non-electrolytes are absorbed to quite a considerable extent, provided their molecules are not so large as to be unable to diffuse through the 'pores' of the swollen exchanger. If an aqueous solution containing an electrolyte and a non-electrolyte is passed through a column of exchanger, the electrolyte appears in the effluent almost immediately; the non-electrolyte may be eluted with water. Thus a very easy separation of electrolytes from non-electrolytes is possible. This is known as 'ion-exclusion' [5]. Since different non-electrolytes are absorbed to different extents, a mixture of various non-electrolytes may, in principle, be separated by a simple chromatographic elution with water (figure 7) [6]. In many cases, however, practical difficulties arise, as the non-electrolytes are all absorbed by the ion-exchanger either too weakly to permit a good separation or too strongly to permit easy elution with water. In the former case, the difficulty is overcome by the use of an electrolyte solution as eluant. The electrolyte 'salts' the non-electrolytes out of solution and

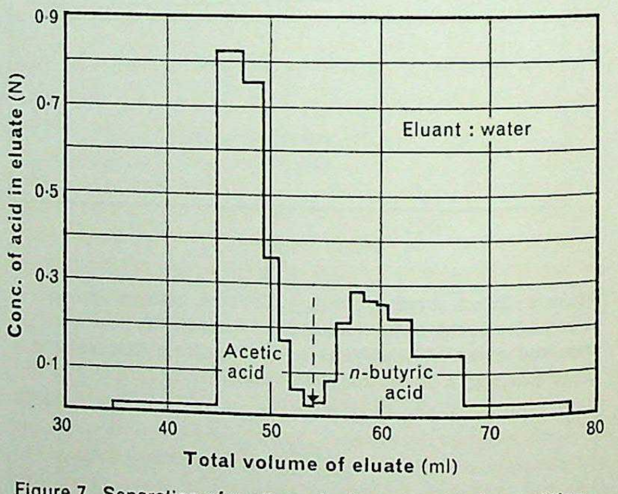

Figure 7 Separation of acetic and *n*-butyric acids by partition chromatography, using a cation-exchange resin.

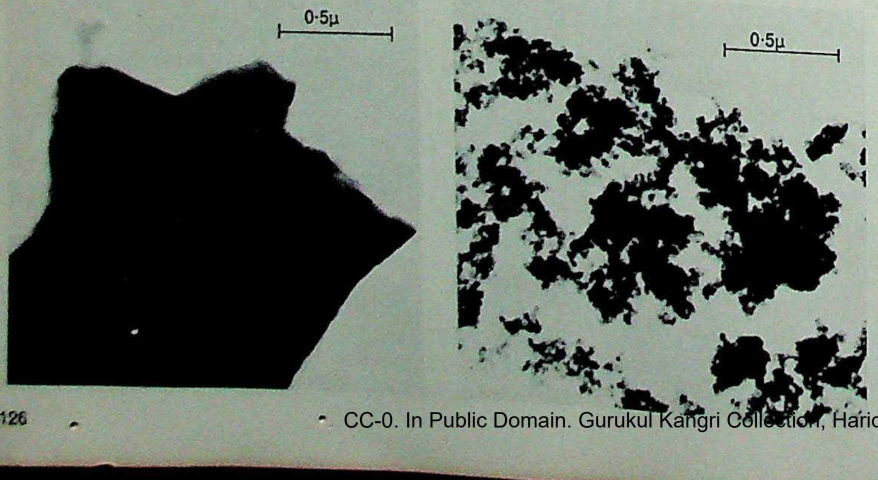

Figure 8 Electron photomicrographs: (left) conventional resin; (right) Amberlyst 15, a macroreticular resin [9].

thus increases their absorption by the resin. This is known as 'salting-out' chromatography. The opposite difficulty is overcome by the use of aqueous solutions of suitable organic compounds as eluants. These increase the solubility of the non-electrolytes in the solution. This is known as 'solubilization chromatography'. Both techniques were developed by W. Rieman [7].

Strong-acid cation exchangers in the hydrogen form and strong base exchangers in the hydroxide form can be used as acid-base catalysts and other ionic forms can occasionally be used [8]. In addition to the advantage of easy removal of the catalyst (by filtration), they are often more effective than mineral acids or alkalies. This is due primarily to the absorption of the organic reactants by the exchanger (mentioned above) combined with the high concentrations of hydronium or hydroxide ions in the exchanger.

Ion-exchange membranes

The discussion hitherto has been devoted primarily to ion exchangers in the form of granular particles, usually spherical. For some purposes, other shapes—rods, fibres, sheets, or belts—are desirable. Exchangers in the form of sheets, usually known as 'ion-exchange membranes', have acquired particular significance in the last ten years. Most of their applications depend on their electrical conductivity. They are usually placed in an electrolytic cell, so as to separate it into various compartments. Owing to the tendency of ion-exchanger materials to exclude excess electrolyte, nearly all the electric current is carried by the counter-ions, and this results in improved current efficiency. Work is proceeding in many countries to develop suitable membranes and cells for the electrolytic desalting of brackish water [10] and even of sea-water. Ion-exchange membranes are also used in fuel cells and some kinds of electrical storage batteries. Normally the electric current is made to pass perpendicularly to the plane of the membrane. S. R. Caplan, however, has developed a particularly interesting technique in which the current passes along the plane of the membrane. This technique can be used for the continuous separation of several ions simultaneously [11].

Inorganic ion-exchangers

The phenomenon of ion exchange was discovered in 1850 by H. S. Thompson and J. T. Way [21] while working with soils containing natural zeolites and most of the early work on ion exchangers was carried out with natural or synthetic inorganic exchangers. Although largely eclipsed by the discovery of ion-exchange resins, interest in inorganic exchangers has revived somewhat in recent years. Potentially, they offer the advantage over organic exchangers of being able to withstand ionizing radiations and much higher temperatures without degradation. In addition, some of them at least, have shown remarkably high selectivity [12]. Thus ammonium phosphomolybdate has a selectivity coefficient, K_{Rb}^{Cs}, in the caesium-rubidium system of about 28; under similar conditions, strong-acid cation-exchange resins show values of only 1·2 to 1·5. Two types of inorganic exchanger have received particular attention:

1. The heteropolysalts, of which ammonium phosphomolybdate is an example. These are undoubtedly crystalline in structure. The crystalline aluminosilicates fall technically into this category, although they are perhaps better known in their own right. Some of them have come into particular prominence as 'molecular sieves' [13].
2. Hydrous oxides and substances such as zirconium phosphate that can be considered as mixed hydrous oxides of elements of groups IV, V, and VI [14]. These are usually regarded as amorphous. They are less selective than heteropolysalts but more selective than ion exchange resins.

Recent developments

In conclusion, two of the most recent fundamental developments deserve mention. Progress in discovering and unravelling the basic interactions underlying ion-exchange selectivity has hitherto been slow. This is because no very satisfactory diagnostic tests were available for deciding which of the various proposed mechanisms were predominant in any particular system. A more decisive stage appears now to have been reached. G. Eisenman [15] has worked out the consequences of the assumption that the cation-exchange equilibria of alkali metals are dominated by the balance between (1) Coulomb interactions between the mobile counter-ions (in various states of hydration) and the fixed groups of the exchanger; and (2) ion-dipole and ion-induced dipole interactions between the counter-ions and water molecules (ionic hydration). Where (1) is weak compared with (2), the 'normal' affinity sequence (Cs > K > Na > Li) is manifested (that is $K_K^{Cs} > 1$, $K_{Na}^{K} > 1$, $K_{Na}^{Cs} > 1$, etc.). As interactions of the first kind increase in magnitude relative to those of the second, a whole series of selectivity 'reversals' are manifested. Eisenman deduced that, provided these are the only two interactions of any consequence, these selectivity reversals will follow a regular sequence. The first to occur is the caesium-potassium reversal giving rise to the sequence K > Cs > Na > Li. This is followed by the caesium-sodium reversal, giving the sequence K > Na > Cs > Li. These are followed in order by K-Na, Cs-Li, K-Li, and Na-Li reversals giving rise finally to the sequence Li > Na > K > Cs (figure 9). (There is a little doubt as to whether the K-Na reversal should precede the Cs-Li reversal.) Eisenman found this pattern experimentally with glass electrodes of various chemical compositions—these are undoubtedly ion-exchangers—and the present author (unpublished work) has confirmed part of this pattern with sulphonated crosslinked polystyrene resins. With some ion-exchange systems, however, other

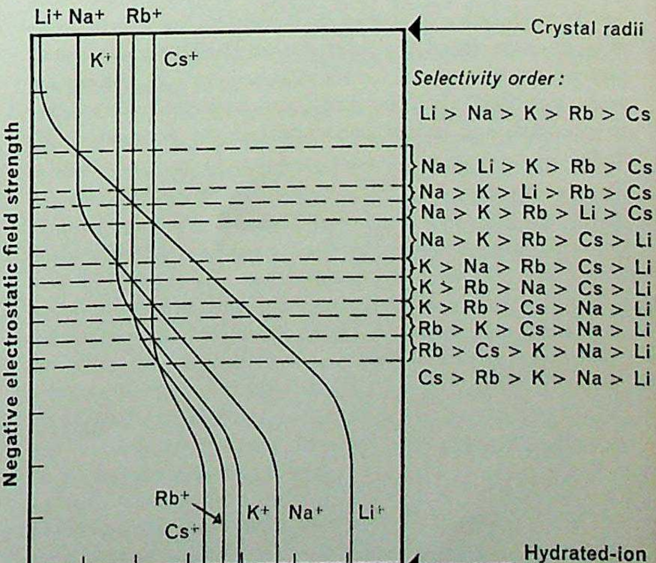

Figure 9 Field strength–ionic radius diagram. (After Eisenman, Rudin, and Casby.)

interactions may be of importance and then affinity sequences other than those predicted and found by Eisenman can occur. For example, where polarization of the fixed groups of the exchanger by the electric fields of the counter-ions is more important than their direct Coulomb interactions (a suggestion due to J. I. Bregman [16]), the order of affinity reversals would be almost the opposite of that described above and would begin with the sodium-lithium reversal. The present author (unpublished work) has found that with some resins containing carboxylate groups, one can obtain the sequence Li > Cs > Na > K. This last sequence indicates the predominance in carboxylic resins of interactions of the type envisaged by Bregman.

The study of affinity reversals is by no means of purely academic interest. This is shown, for example, by the fact that the chemoreceptors on the taste-bud surfaces of rodents show the sensitivity order Li > Na > K, whereas those of carnivores show the order K > Na > Li [17]. Ionic transport, accumulation, and selectivity in biological systems have intrigued physiologists for many years and a number of theories and 'models' have been proposed to account for the phenomena. Most of these suggestions involved either ionic 'carriers' or ionic 'pumps' and their weakness lay partly in the fact that, with possibly a few exceptions, no experimental models could be found to demonstrate their operation. Commencing with the study of membrane potentials across frog sartorius muscles [18], G. N. Ling has accumulated an impressive amount of evidence in favour of his 'fixed-charge' hypothesis. In brief, this amounts to the statement that ionic transport and accumulation in biological systems proceed via the diffusion of ions through, and interactions of ions with, systems containing both covalently bound groups bearing electric charges and mobile counter-ions. Such systems are, of course, ion exchangers. The great strength of Ling's approach is that it is based on systems and phenomena which, so far from being hypothetical, are well-established experimentally. This, of course, does in itself not prove the correctness of his views, and the controversy will doubtless continue. The problems involved are of great complexity and a fascinating and detailed discussion of them has been given by Ling in a recent monograph [19]. Work on the properties of ion exchangers with structures more akin to those found in living systems should greatly clarify present-day concepts. If Ling's views are justified, the phenomena associated with ion exchangers may turn out to play an essential, and indeed major, part in the processes of life itself.

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Microwave spectroscopy

T. M. Sugden

The absorption of electromagnetic radiation of wavelength between 10 cm and 1 mm by gases arises in the main from changes in molecular rotational energy. Spectra of this absorption can be used to obtain moments of inertia of the molecules, and hence bond lengths and angles. Valuable further applications give information about dipole moments, the electronic structure of bonds, and barriers to internal rotation in molecules, for which few alternative methods are available.

The development of spectroscopic techniques for a new region of wavelengths always provides a rich harvest of information. This has proved to be singularly true for the microwave region, which may be defined as that part of the electromagnetic spectrum with wavelengths between 10 cm and 1 mm *in vacuo*. Microwaves were first used for communications on a large scale in World War II, and this led to improved and reliable methods for their production, manipulation, and detection. The application to molecular spectroscopy is almost entirely a post-war development.

The internal motion of a molecule is compounded of electronic movement; of vibration of the nuclei in the field of the electrons; of end-over-end rotation of the nuclei—here called simply molecular rotation; and of nuclear spin. The frequencies of these various motions are so different that, to a fair approximation, they can be considered as independent, and specific amounts of energy can be assigned to each motion. All of them are quantized, that is, their energies are restricted to certain values, called energy levels. Transitions between these can occur by absorption or emission of a quantum of radiant energy $h\nu$ (h is Planck's constant and ν the frequency of the radiation), producing characteristic spectra. In particular, differences of molecular rotational energy correspond with microwave quanta, and it is with these differences that the great bulk of microwave spectroscopy deals.

The classification of rotors

If a rotor is made up of a series of mass points $m_1, m_2, \ldots$, rigidly connected, at respective perpendicular distances $x_1, x_2, \ldots$, from a line, the moment of inertia about that line is defined as $\Sigma_i m_i x_i^2$. There are always three such lines, or axes, called the principal axes, with corresponding moments of inertia I_A, I_B, I_C, labelled according to the following rules [1]. The axes are mutually perpendicular and pass through the centre of gravity, and I_A is the smallest possible moment of inertia, I_C the largest, and I_B intermediate, if they are unequal. These moments are called principal moments of inertia, and on them is based a general classification of rotors. Various types of molecule, considered as rigid rotors, fall into these classes.

1. Spherical tops, for which $I_A = I_B = I_C$. Highly symmetric molecules of cubic or octahedral type, such as CH_4 and SF_6, fall in this category.
2. Symmetric tops, for which $I_A < I_B = I_C$ or $I_A = I_B < I_C$. The former are designated prolate (cigar-shaped) and the latter oblate (pancake-shaped). Molecules with a single n-fold symmetry axis, where $n \geqslant 3$, form this class; examples are PCl_3, CH_3Cl, SF_5Cl (which has a 4-fold axis $F(SF_4)Cl$).
3. Linear molecules are a special sub-class of symmetric tops for which $I_A = 0$ and $I_B = I_C$. Examples are CO_2, OCS, C_2H_2.
4. Asymmetric tops, for which $I_A < I_B < I_C$. Most molecules, including some very simple ones, fall into this group; examples are H_2O, CH_2O, CH_2Cl_2, CH_3CHO.

The energy levels of rigid rotors

The application of quantum mechanics to a rotating body [2] shows that its total angular momentum **J** is restricted to values

$$\mathbf{J} = \frac{h}{2\pi}\sqrt{\{J(J+1)\}}$$

where J is a quantum number, which for molecules without unpaired electrons, in effect nearly all molecules, takes integral values 0, 1, 2, 3, . . .

The energy levels W_J associated with this angular momentum depend on the type of rotor. For linear molecules they are given by

$$W_J = hBJ(J+1)$$

where $B = h/8\pi^2 I$, I being the single moment of inertia [3]. A similar expression holds for spherical tops. For symmetric tops, the rotation has a restriction on it, because of the strong directional field along the symmetry axis. The projection of **J** along this axis must be $\mathbf{K} = \pm(h/2\pi)K$, where K is a second quantum number which can assume values 0, 1, 2, . . . , J. The levels are now characterized by J and K, and are [3]:

$$W_{JK} = hBJ(J+1) + h(C-B)K^2 \quad \text{(oblate)}$$
$$W_{JK} = hBJ(J+1) + h(A-B)K^2 \quad \text{(prolate)}$$

A, B, C are related to the principal moments of inertia by $A = h/8\pi^2 I_A$, and so on.

The solution of the wave-equation for asymmetric tops does not lead to energy levels that can be expressed in terms of A, B, and C in simple analytic form. The approximate distribution can be seen from figure 1. This diagram represents the behaviour of the lower energy levels when B is varied from the limiting prolate condition ($A > B = C$) to the limiting oblate one ($A = B > C$). All symmetric-top levels in which $K \neq 0$ have double degeneracy—that is, they occur twice—corresponding classically with rotation about the symmetry axis in opposite directions. This degeneracy is removed when the top becomes asymmetric. A level is designated by $J_{K_{-1}K_1}$, where K_{-1} and K_1 are respectively the K values of the level in the limiting prolate and oblate symmetric tops. Detailed tabulations of levels exist for all degrees of asymmetry [3].

Rotational spectra of rigid rotors

For a rotating molecule to give an absorption spectrum, it must have a permanent electric, or very occasionally magnetic, dipole, so that it can interact with radiation of frequency ν, related to a pair of energy levels by Planck's law

$$W_2 - W_1 = h\nu$$

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Thus spherical tops do not give rotational spectra. The possible transitions for other types are restricted by quantum-mechanical selection rules. Thus, for linear molecules and symmetric tops the change in J, called ΔJ, can only be ± 1 or occasionally 0, and for the latter $\Delta K = 0$. For asymmetric tops, $\Delta J = 0$ also occurs: the additional restrictions on ΔK_{-1} and ΔK_1 are too elaborate to be treated here [3].

The energy levels, transitions, and spectrum of a linear rotor are shown in figure 2. The spectrum consists of lines of frequency $2B(J+1)$, for the transitions $J \to J+1$, separated by $2B$. Consider a typical diatomic molecule, with $I = 10^{-38}$ g cm^2. Then $B \sim 8 \times 10^9$ sec^{-1}, and lines are separated by $1{\cdot}6 \times 10^{10}$ sec^{-1} (= 16 000 Mc/s), while, for example, the $J = 1 \to 2$ line has a frequency of 32 000 Mc/s ($4B$). This latter corresponds with a wavelength of 0·94 cm *in vacuo*. This simple calculation suffices to show that the bulk of molecular rotational spectra will fall in the microwave region.

The rotational spectra of linear and symmetric-top molecules are thus predicted to be very simple, and this turns out to be so, although they are not quite as simple as this elementary treatment suggests. The identification of the J value for an observed transition, however, presents little difficulty. This identification is more difficult for an asymmetric-top transition because of the irregular pattern of the energy levels, but is generally possible. Values of B may then be derived for linear and symmetric tops, and of A, B, and C, in general, for asymmetric tops.

Techniques of microwave spectroscopy

Microwave spectrometers incorporate the rather novel device of continuous variation of the frequency of the source, essentially monochromatic at any one instant, across the spectral region, in contrast with the methods of optical spectroscopy. The radiation is passed through a cell containing the gas being studied, and the absorption is recorded. Figure 3 shows the simplest type, known as a video spectrometer [3]. The source is a klystron valve, which, with fixed potentials on its electrodes, feeds a few milliwatts of microwave power of fixed frequency into a waveguide. This frequency can be modulated electrically over a range of about 50 Mc/s by applying a periodic voltage of sawtooth form to one of the electrodes (the reflector). The repetition frequency of this modulation is usually low, sometimes only one cycle in several seconds. Simultaneous application of the sawtooth signal to the X-plates of an oscillograph provides an uncalibrated abscissa of klystron frequency.

The waveguide is a rectangular metal tube, whose cross-sectional dimensions a and b roughly fulfil the rule $\lambda > a > \lambda/2 > b$, where λ is the wavelength of the radiation. Some of the radiation is diverted into a side waveguide for frequency measurement. The remainder traverses the absorption cell, which is a length of waveguide with vacuum-tight mica windows. This cell contains the gas under study, at a pressure of about 10^{-2} mm of mercury. The emerging radiation falls on a silicon crystal with a fine metallic whisker contact, where it is rectified, passed to an amplifier, and thence to the Y-plates of the oscillograph, whose trace discloses the presence of any absorption lines in the range of frequency being covered.

A mechanical tuning device on the klystron allows successive regions to be swept by the sawtooth voltage up to a total of about 15 per cent of the absolute frequency. About seven klystrons are required to cover the range of 15 000–40 000 Mc/s (2 cm to 0·75 cm in wavelength).

The absorption lines are generally weak. They become stronger with pressure, but only up to pressures of about 10^{-2} mm of mercury. At higher pressures, interactions between neighbouring molecules cause significant modifications of the rotational levels, and broaden the lines rather than cause an increase in amplitude, so reducing the resolution. Indefinite extension of the absorption cell is not possible, because of transmission losses in the guide. Lengths of about 20 m, suitably coiled, have been used. The strongest lines then give a few per cent absorption, and observations can be made down to about

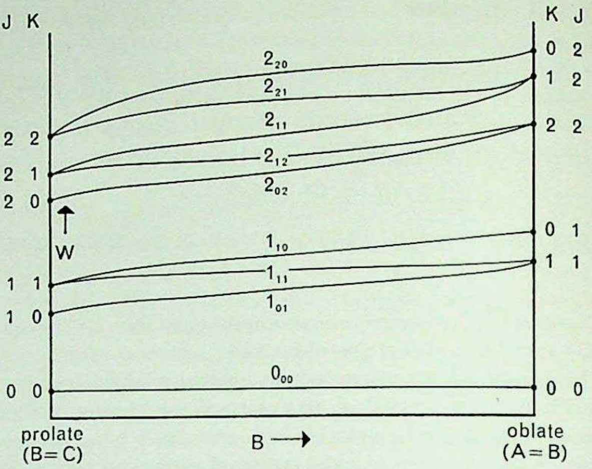


Figure 1 Energy levels of asymmetric top (diagrammatic).

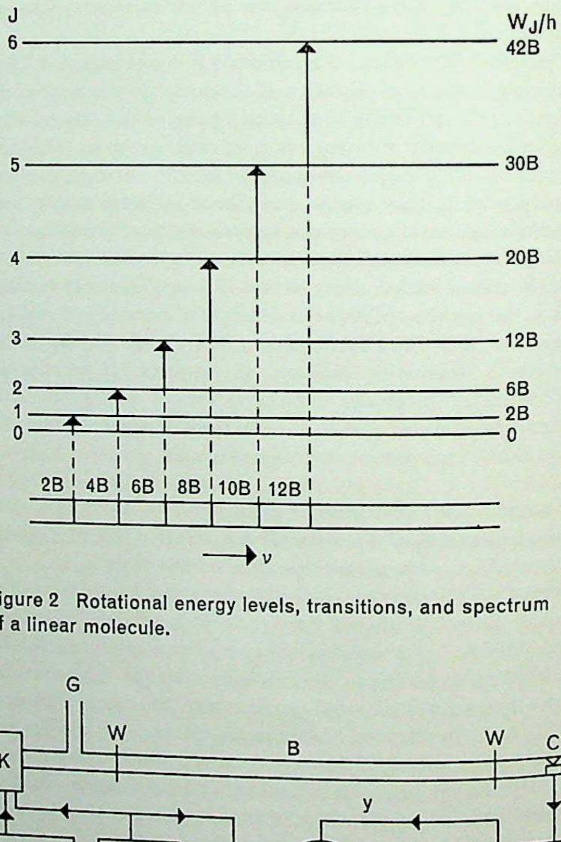


Figure 2 Rotational energy levels, transitions, and spectrum of a linear molecule.

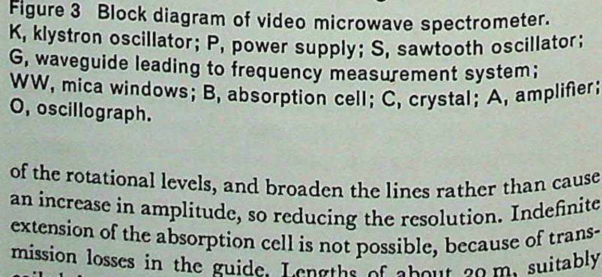


Figure 3 Block diagram of video microwave spectrometer. K, klystron oscillator; P, power supply; S, sawtooth oscillator; G, waveguide leading to frequency measurement system; WW, mica windows; B, absorption cell; C, crystal; A, amplifier; O, oscillograph.

0·01 per cent absorption with video instruments. Methods for improving this will be described later.

An outstanding advantage of microwave spectroscopy over techniques for shorter wavelengths is the accuracy of frequency measurement. A quartz crystal oscillator is brought accurately to, say, 5 Mc/s by matching with a similar standard frequency such as the signal broadcast by the General Post Office from Rugby, England, and checked by the National Physical Laboratory. This is accurate to at least 1 part in 10^8. Electronic multipliers are then used to provide a series of higher frequency signals at, say, 60, 180, 540, 1080 Mc/s, and these are fed simultaneously into a silicon crystal in the side-arm of the waveguide. Higher harmonics are generated in this crystal, and give beat-frequency signals with the microwaves from the klystron. The system then provides a series of accurate marker frequencies at multiples of 60 Mc/s, correct to about 1 part in 10^7. Conventional radio techniques can be used to measure the frequency difference between an absorption line and an adjacent, known, harmonic of 60 Mc/s. Absorption frequencies are quoted to six or seven significant figures.

Wavelengths shorter than about 8 mm are generated harmonically. Radiation from a klystron at, say, 12 mm falls on a crystal rectifier and whisker in a waveguide. This is a non-linear device and thus produces harmonics of the incident frequency. Power at these higher frequencies, with wavelengths of, for example, 6, 4, and 3 mm, is led away along waveguides too small to transmit the fundamental. In this way, wavelengths of down to 0·5 mm have been produced for spectroscopic purposes [4]. Power is low because of losses at generation, and manipulation of very short microwaves is difficult. Fortunately, however, the intensities of absorption lines rise roughly as the cube of the frequency, and this offsets some of the difficulties.

Molecular geometry, isotope effects, and non-rigidity

Rotational parameters A, B, and C, and hence moments of inertia, are thus obtained to six significant figures. A linear molecule, such as OCS, requires two internuclear distances for complete specification, whereas a particular isotopic species yields only one B value. Use of a different isotopic species, having the same internuclear distances but a different mass, should yield a second B value, and hence both internuclear distances could be obtained. A similar procedure can be envisaged for molecules with more geometrical parameters. Lines from natural concentrations of isotopic species can often be observed with sensitive instruments.

Unfortunately, straightforward application of this principle leads to complete confusion, different results being obtained from different combinations of isotopic species. For example, the results from $^{16}O^{12}C^{32}S$ and $^{16}O^{12}C^{34}S$ lead to bond lengths $r_{CO} = 1{\cdot}1647$ Å and $r_{CS} = 1{\cdot}5576$ Å, while those from $^{16}O^{12}C^{32}S$ and $^{18}O^{12}C^{32}S$ give $r_{CO} = 1{\cdot}1552$ Å and $r_{CS} = 1{\cdot}5653$ Å. These disturbing effects arise from the lack of rigidity of the molecule, which affects the rotational energy levels for two reasons. The first of these is centrifugal stretching, a tendency for the molecule to become larger because of centrifugal forces. This is a very small effect, except at high J values, and can usually be allowed for quite easily [3]. The second effect arises because the molecule is vibrating with zero-point energy, a half-quantum of vibrational energy, in its lowest vibrational energy level. Consequently, the quantities such as A obtained from the microwave spectrum represent the reciprocal moment of inertia averaged over the zero-point vibration. Because of the difference of isotopic masses, the zero-point vibrations for different isotopic species are not quite the same, and consequently the values of A derived for them are not directly comparable.

This effect can be allowed for in two ways. Vibrationally excited molecules give rotational spectra that are slightly displaced (by amounts of 10–100 Mc/s per vibrational quantum) from those of the zero-point vibrating molecule. If such spectra can be identified, an extrapolation can be made to a hypothetical non-vibrating molecule, to which the isotopic substitution law applies with accuracy. This is possible only for simple molecules, such as OCS, with small numbers of vibrational modes. A less accurate, but more widely applicable, method involves very extensive isotopic substitution. The results for B from zero-point $^{16}O^{12}C^{32}S$ and $^{16}O^{12}C^{34}S$, for example, can be used to calculate the distance of the S atom from the centre of gravity of each molecule, rather than the bond lengths r_{CO} and r_{CS} [1, 5]. This calculation is the more accurate, because the centre of gravity migrates towards the heavier isotope on substitution. Similar calculations are made for the C atom with $^{16}O^{12}C^{32}S$ and $^{16}O^{13}C^{32}S$, and for the O atom with $^{16}O^{12}C^{32}S$ and $^{18}O^{12}C^{32}S$, and all the results combined to give values of r_{CO} and r_{CS}. This method is capable of giving bond lengths consistent to within 0·005 Å, and corresponding accuracy in bond angles. This accuracy is rather higher, for bond lengths, than that obtained with diffraction techniques and considerably better for angles. Where spectra are weak, or where natural concentrations of rarer isotopes are small, much preparative work may be required to obtain a complete molecular structure. Nevertheless, a large number of molecules have been analysed by this technique.

The molecular Stark effect and dipole moments

Quantum mechanics imposes a further restriction on molecular rotation. The projection of the total angular momentum $\mathbf{J}$ along a particular direction in space is restricted to values $\mathbf{M}_J = (h/2\pi)M_J$, where $M_J = J, J-1, J-2, \ldots, -J$ [2]. In the absence of applied fields, these $2J+1$ possibilities have the same energy, and are said to be degenerate. Some field is necessary in order that the molecule shall 'feel' the imposed direction, and the most usual is an electric field, which interacts with the electric dipole moment μ of the molecule. The interaction energy is given by $-\mu E \cos\theta$, where E is the field strength and θ the angle between the directions of E and μ. This angle is restricted to certain values corresponding with the various values of M_J. Consequently, the rotational energy takes somewhat different values for these various possibilities, that is the degeneracy is lifted, the ordinary rotational levels are split, and the ordinary rotational lines become groups of lines. This is called the 'molecular Stark effect'.

For symmetric tops with the quantum number $K \neq 0$, μ, which is always directed along the symmetry axis, has a component along the direction of $\mathbf{J}$, which is fixed in space because of the conservation of angular momentum. This component interacts directly with the field E in one of the $2J+1$ orientations of $\mathbf{J}$ to give a 'first-order Stark effect'—one proportional to μE. All other cases give an average value of zero for the component of μ along $\mathbf{J}$ over a rotation, except in so far as the interaction of μ with the field perturbs the rotational motion. This perturbation, which occurs because some orientations of μ with respect to E are more stable than others, results in a small net effective dipole in the direction of E proportional to $\mu^2 E$, and thus in an interaction energy proportional to $\mu^2 E^2$, which is known as a 'second-order' Stark effect [3].

The constants of proportionality are known functions of quantum numbers, and hence measurements of Stark effects lead to values of dipole moments. The method is accurate, and it has the advantage that it can be applied to relatively involatile materials, such as salts at temperatures of a few hundreds of degrees Centigrade, and in the presence of polar impurities.

The field is applied to an electrode mounted as shown in figure 4a, across the waveguide cell. Fields of 50 volts per cm are usually adequate for first-order effects, while 2000 volts per cm may be required to give the necessary splitting of a few Mc/s with second-order effects.

The Stark effect is used to advantage in the most common kind of microwave spectrometer. The field is applied to the electrode as a square-wave signal of frequency about 100 kc/s, as shown in figure 4b, so that the receiving crystal 'sees' the spectra of polarized and unpolarized molecules alternately. Highly selective amplification at this frequency is used. The oscillograph displays both spectra simultaneously [3].

Nuclear electric quadrupole effects and electronic structure

Atomic nuclei have a spin angular momentum

$$\mathbf{I}=(h/2\pi)\sqrt{\{I(I+1)\}}$$

I being a quantum number with a half-integral value from zero upwards. It has a fixed value for each type of nucleus. For example, I is zero for ^{12}C, ^{16}O; $\frac{1}{2}$ for ^{1}H, ^{13}C, ^{15}N; 1 for ^{2}H, ^{14}N; and $\frac{3}{2}$ for ^{35}Cl, ^{37}Cl. Nuclei with $I>\frac{1}{2}$ behave as non-spherical ellipsoids of revolution, and are said to have electric quadrupole moments (eQ) [3].

The extra-nuclear electrons give a field of average gradient q at the nucleus, generally dependent on direction. The interaction energy of the quadrupole with this is eQq, for q along the direction of the nuclear axis. The most important atomic orbitals are of type s (spherically symmetrical) and p (cylindrically symmetrical), shown in figure 5. The former gives zero q at the nucleus, and the latter finite q, with a value q_{at} along the axis of the orbital (and $-\frac{1}{2}q_{\mathrm{at}}$ perpendicular to it). For a p electron, the energy eQq depends on the orientation of the nucleus to the orbital, and quantum treatment shows that $I+1$ coupling energies are allowed. The coupling energy eQq_{at} of a p electron in an isolated atom varies between zero and the equivalent of 10^3 Mc/s for various species, and may be found from atomic spectra.

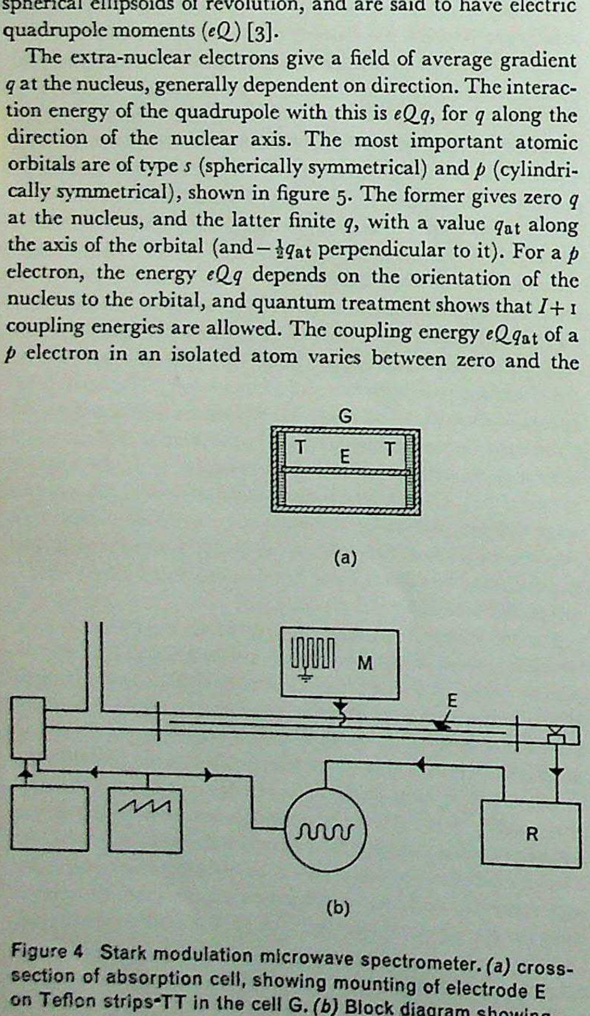


Figure 4 Stark modulation microwave spectrometer. *(a)* cross-section of absorption cell, showing mounting of electrode E on Teflon strips TT in the cell G. *(b)* Block diagram showing ground-based 100 kc/s square-wave modulator M, electrode E, and tuned amplifier R. Other components as in figure 3.

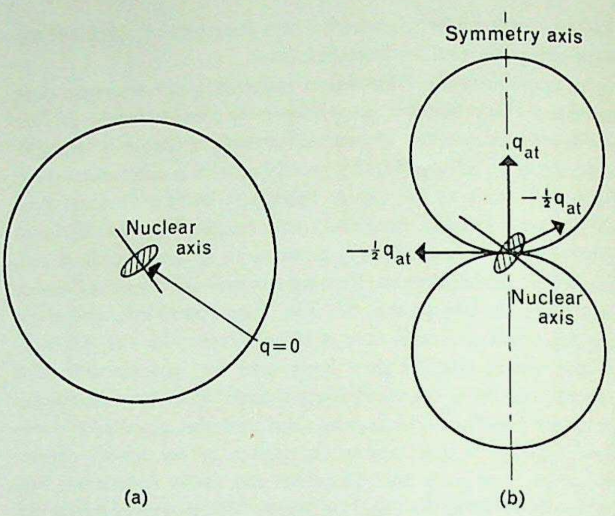


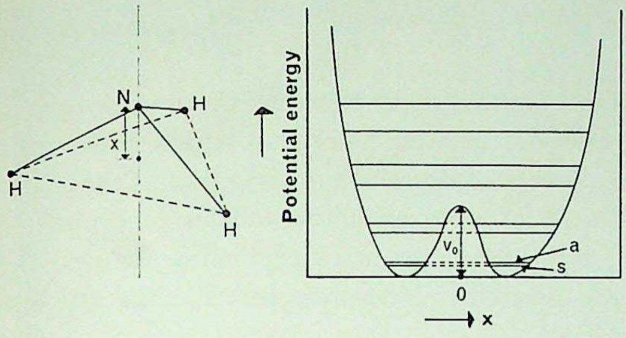
Figure 5 *(a)* Polar diagram of an s orbital (spherically symmetrical); $q=0$ at the nucleus. *(b)* Polar diagram of a p orbital (cylindrically symmetrical); $q=q_{\mathrm{at}}$ along the axis and $-\frac{1}{2}q_{\mathrm{at}}$ perpendicular to it. Both diagrams show a quadrupolar nucleus.

When a molecule containing a quadrupolar nucleus undergoes a rotational transition, simultaneous changes in quadrupole coupling energy occur, producing a hyperfine structure of the rotational spectrum. From this, a molecular eQq value can be deduced, which is generally different from the atomic eQq value, because the atomic orbitals have been modified by bonding. The modifications have been described, not completely satisfactorily, through two concepts—ionicity, whereby a greater or smaller 'fraction' of an electron is assigned to an atomic orbital on bond formation, and hybridization, whereby an atomic orbital compounded of various fractions of basic s, p, and higher, orbitals is allowed in a molecule [6, 7].

Both factors affect the quadrupole coupling of a nucleus, and the unravelling of their respective contributions has proved awkward, requiring additional empirical equations. Gross features can be quite revealing, however, as is shown by the following values for ($eQq_{\mathrm{mol}}/eQq_{\mathrm{at}}$) for some chlorine compounds—NaCl($<0{\cdot}01$); TlCl ($0{\cdot}144$); CH_3Cl ($0{\cdot}68$); ICl ($0{\cdot}75$); FCl ($1{\cdot}33$). In each case, eQq_{at} is $109{\cdot}6$ Mc/s. A Cl^- ion has a closed shell of 6p electrons in three perpendicular orbitals, which is spherically symmetric, with $eQq=0$, while a Cl atom has one gap in this, giving $eQq=-109{\cdot}6$ Mc/s The trend from pure ionic to nearly covalent bonding from NaCl to ICl is evident from the data. The high value for FCl occurs because of a contribution from F^-Cl^+, in which charge has actually been removed from a p orbital of the Cl atom.

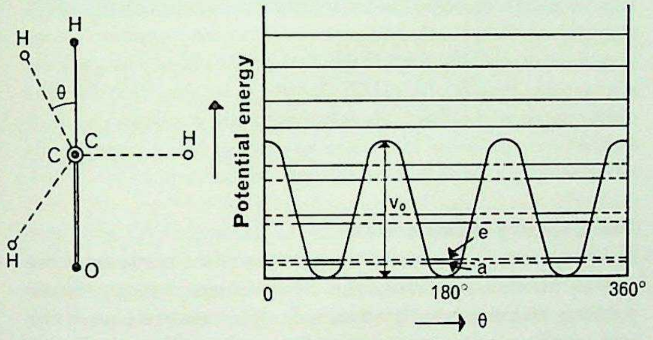
Inversion, restricted rotation, and potential barriers

Figure 6a shows an ammonia molecule, which has a stable pyramidal configuration. The change of potential energy as the N atom moves across the plane of 3H is depicted in figure 6b, and there is a potential barrier V_0 between the two equivalent equilibrium configurations. This barrier produces a grouping of the vibrational levels in pairs, particularly marked for the two lowest, labelled s and a. These would be degenerate if V_0 were infinite, corresponding with equivalent vibrations in independent potential wells. When V_0 is not infinite, there is a quantum-mechanical interaction between the equivalent configurations which allow the N atom to cross the plane even



(a) (b)

Figure 6 *(a)* Ammonia molecule. x= distance from the N atom to the plane of the H atoms. *(b)* The potential energy of NH_3 as a function of x, and associated energy levels.



(a) (b)

Figure 7 *(a)* Acetaldehyde molecule viewed along the C—C bond; CH_3 bonds are dotted. *(b)* The potential energy of internal rotation as a function of θ, and the associated energy levels.

when the vibrational energy is less than V_0. This is called inversion, and is an example of quantum-mechanical tunnelling, a process of transition forbidden in classical mechanics because of insufficient energy to surmount the barrier. It is associated with a transition between s and a falling in the microwave region, and gives a strong absorption spectrum, which was observed by C. E. Cleeton and N. H. Williams in 1934 [8], and was, in fact, the first one to be observed. The energy difference between a and s is a sensitive function of V_0, which is calculated from it to be 5962 cal mole^{-1}. The inversion frequency has been used to provide a time standard in the ammonia clock, and the transition in emission was used to operate the first masers [3].

A closely related phenomenon is restricted rotation. Figure 7a shows a molecule of acetaldehyde, CH_3CHO. Rotation of the CH_3 group with respect to the CHO group is described by the angle θ. The interaction between the groups has a potential energy with a three-fold maximum V_0, as shown in figure 7b. This results in the lower energy levels being those of torsional oscillations rather than full rotations. Again, because the barriers are not infinite, the lower levels are in narrowly separated pairs, rather than being three-fold degenerate. Quantum-mechanical tunnelling occurs through the barriers and shows itself spectroscopically in two ways, by a spectrum arising from internal motion alone, sometimes in the microwave region, and by a fine structure of the ordinary rotational spectrum, because of simultaneous changes in total and internal rotation. The separation of the levels a and e can be found, and it is a very sensitive function of V_0, which is hence determined.

Of the few methods available for measurement of barrier heights in molecules, the microwave method is easily the best.

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The cell cortex

A. S. G. Curtis

The recent progress in understanding the mechanism of heredity in terms of the nucleic acids may well distract attention from the possibility of other self-replicating mechanisms for inheritance. This article describes experiments that show that the cell cortex controls the organization of the fertilized cell in amphibia—an action that has long been known for protozoa. These delicate experiments in grafting portions of a cell are being continued to see if the cell cortex is self-replicating, as well as being a controlling agent and the significance of this possibility is also discussed in the article.

The cortex or 'rind' of a cell is the outer part of the cytoplasm and includes the cell membrane, the plasmalemma. This definition is not precise, but it conveniently describes a set of structures that have the common property of controlling the development of the embryo to a considerable extent. Although a cortical reaction occurs in many eggs on fertilization, this will not be discussed, as it is probable that rather different structures are involved.

It was gradually realized in the 1930s that one or more factors essential for the correct development of the embryo were probably located either in or very close to the surface of the fertilized egg. They were termed cortical factors. J. Pasteels [1] showed that this was so for a variety of species of Amphibia, and C. P. Raven [2] demonstrated this in the eggs of *Lymnaea stagnalis*, a pond-snail. Both of these workers centrifuged the eggs, which considerably disturbed the structure of the cytoplasm and position of the nucleus. Nevertheless, the eggs developed either normally, or very nearly so. It was argued that, since the cortex was the only part of the egg cell undisturbed by mild centrifugation, the system that produces the specific arrangement of the various parts of the embryo must reside in the cortex. Pasteels [3] followed up this work with a series of more controlled disarrangements of the inner cytoplasm that suggested that one particular region of the cortex played a most important part in controlling development. This region is known from its appearance as the grey crescent. Some years earlier F. Seidel [4], working with the eggs of the damsel-fly *Platycnemis pennipes*, had shown that one region of the egg, close to or including the surface, contained a factor essential for 'activating', as he described it, the nuclei; development did not ensue unless this activation occurred.

Despite this evidence for a cortical control system in widely different animals, it remained possible that the system resistant to centrifugation, which plays so large a part in the control of embryogenesis, was to be identified with some region of the egg other than the cortex. For example, it was suggested that the nucleus or nuclei had the ability to set up mechanisms that would bring about the spatial co-ordination of the development of the various parts of the embryo into the correct structures. The experimental test of the cortical theory is to graft pieces of cortex from one part of the egg to another, or to remove certain pieces. Alterations or deficiencies in the embryos produced by such operations would confirm the existence of cortical factors.

In fact this type of experiment had already been carried out on various protozoons—on *Stentor* spp. in particular. V. Tartar [5] described his own work and that of other workers on these animals, and this clearly demonstrates, by grafting experiments, that the cortex plays a most important part in the control of the complex and beautiful pattern of cilia and pigment which they bear. This work also showed that one portion of the cortex, that associated with the oral primordium (which gives rise to the mouth), is chiefly involved in this control. The cortex in these animals has self-replicating properties. Nevertheless the situation in protozoons may not necessarily be paralleled by that in higher animals, metazoons.

Micro-surgery on the cortex

In 1960, I succeeded in grafting portions of the cortex from one cell to another—probably the first example of cytoplasmic grafting in metazoa [6] (figure 2). The material used was fertilized eggs of the South African clawed toad *Xenopus laevis*. In view of Pasteels's work, the first experiment was to test the hypothesis that A. Dalcq and he had advanced [7], namely that the interaction of some cortical factor, centred on the grey crescent, with another factor in the cytoplasm was essential for the occurence of gastrulation in amphibia. Gastrulation involves cell movement and the passage of a chemical stimulus, an inducer, from one set of cells to another. It brings about the first obvious appearance of the symmetry of the animal, arranges the main disposition of organs, and leads to the differentiation of a nervous system and associated structures.

Initially this hypothesis was tested by grafting cortex from the grey crescent region of uncleaved fertilized eggs to the opposite side of a second egg, so that the egg receiving the graft had two grey crescents on opposite sides (figure 1). This graft caused the embryo to develop two separate sets of gastrulation movements and to produce two separate primary nervous systems with associated structures (figures 3 and 4). As a result the eggs developed into double embryos, joined Siamese-twinwise by their belly regions. The graft had induced those regions of the fertilized egg that would have otherwise become parts of the abdomen to form complete nervous systems with their associated musculature, sense organs, and skeletal

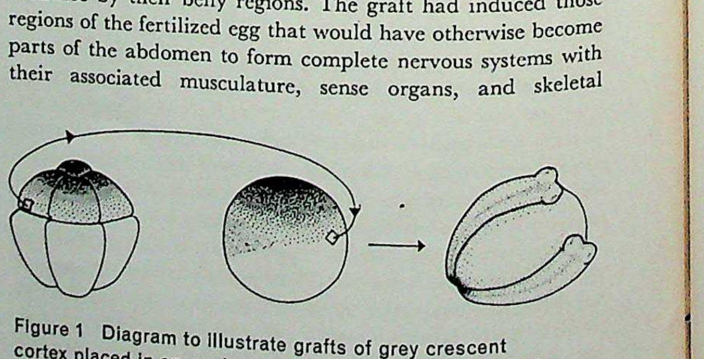

Figure 1 Diagram to illustrate grafts of grey crescent cortex placed in an uncleaved fertilized egg. This egg will acquire two grey crescents, leading to the production of a secondary embryo which is twinned with the normal one. Graft may come from any stage between 1 and 8 cells.

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Was educated at King's College, Cambridge. He took his Ph.D. at Edinburgh, working in the Institute of Animal Genetics, in 1957. From 1957 till 1962 he carried out research on the surface properties of embryonic cells in the Department of Anatomy, University College, London. He moved to the Department of Zoology, University College, London, as Lecturer in Zoology, in 1962, where he has continued his research into a variety of cell-surface properties.

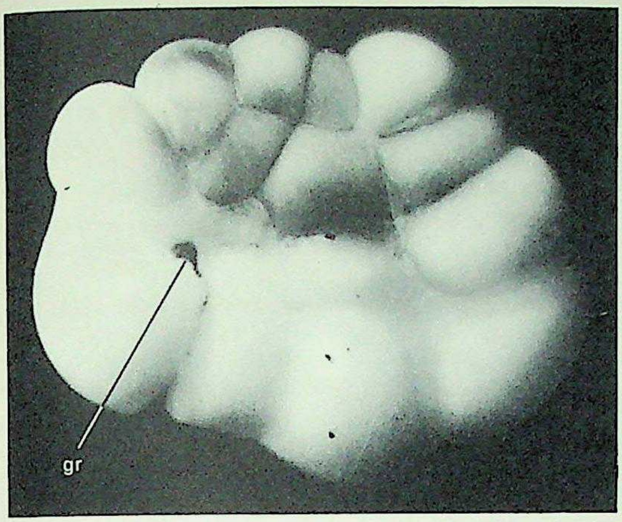

Figure 2 Graft (gr) placed in 8-cell embryo viewed at 16-cell stage. *X. laevis*. Graft has contracted in size just after grafting, making it appear very dark. This contraction is normal and is followed by an expansion. Ultimately the graft appears to merge into its surroundings.

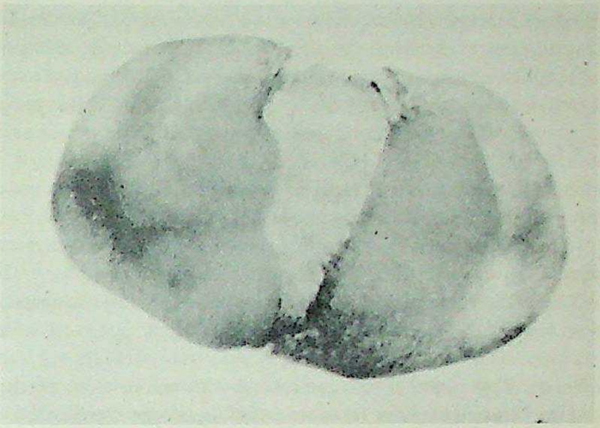

Figure 3 General view (×30) of embryo developing from grey crescent graft at earliest neurula stage. At either end the neural folds are rising. The left-hand set belong to the normal embryo. The right-hand set belong to the induction resulting from the graft.

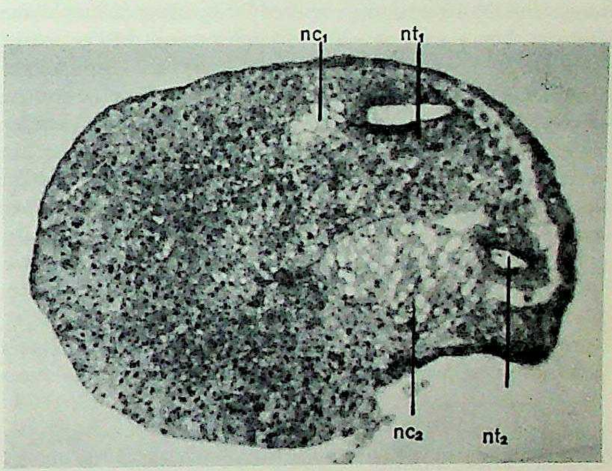

Figure 4 Section through grafted embryo at rather later stage than Fig. 3 (×70). Twin nervous systems, notochords, and associated musculature are visible. nc_1, host notochord; nt_1, host neural tube; nc_2, graft induced notochord; nt_2, graft induced neural tube. Stained celestin blue and eosin.

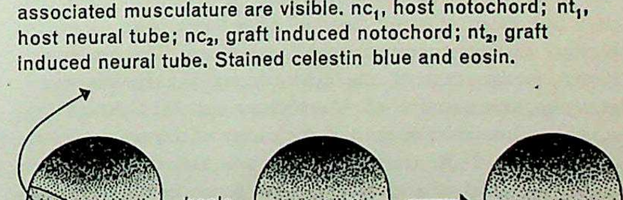

Figure 5 Diagram to illustrate effect of excising grey crescent cortex from uncleaved fertilized egg.

structures. Such grafting experiments lead us to believe that the grey crescent cortex acts to produce the dorsal lip. This plays the most important role in gastrulation and is the source of the inductive chemicals that in turn lead to the formation of a nervous system. The grey crescent region of the egg lies at the site of the future dorsal lip.

H. Spemann and H. Mangold [8] made the fundamental discovery of the induction process that takes place at gastrulation and is essential for normal development. For some long while after this discovery it seemed that this induction was the first act of differentiation. Nevertheless, this discovery left unsolved the nature of the preceding interactions that were essential for the establishment of the dorsal lip and for the distribution of various types of cell property in the parts of the embryo that govern the complex and orderly cell movements involved in gastrulation. Work on the properties of the amphibian cortex is beginning to suggest answers to these problems.

Confirmation of the existence of the special properties of the grey crescent cortex was obtained by excising this region from fertilized uncleaved eggs [9]. The result of this operation is that, although cleavage and mitosis continue unimpaired, there is no development of embryonic structure at all (figure 5). Related experiments suggest [10] that one of the differentiated characters deleted by this operation is that of the surface differences in cells that are thought to be responsible for the gastrulation movements [11].

The grey crescent cortex of the eight-cell embryo still possesses the ability to carry out inductions if grafted to younger embryos; it has not, therefore, lost its morphogenetic properties at this stage. But the embryo of this age has lost its ability to react to grafts. In addition, excision of the grey crescent from an eight-cell stage has little or no effect on development, as the missing crescent properties are replaced from nearby cortical regions. These results indicate that there has been some change in the cortical organization between the two-cell and eight-cell stages. Recent experiments suggest that this change spreads across the surface of the egg, starting from the grey crescent. When it is complete, interactions can take place between various parts of the cortex. These will tend to suppress the effects of additions—grafts—and to replace missing parts—the results of excisions. This change also appears to be closely connected with the determination of the axes of symmetry of the embryo [9]. A similar system of self-regulating control of cortical pattern may occur in protozoons, according to E. Fauré-Fremiet [12]. Thus these experiments reveal that there is a pregastrular morphogenesis of the embryo and suggest that interesting biophysical problems are inherent in the nature of the cortex.

In amphibia, other regions of the cortex seem to be comparatively unimportant in the initiation of morphogenesis. Removal of large pieces of the cortex from all regions other than the grey crescent, or the grafting into these regions of non-grey crescent material, has no effect on the determination of gastrulation. However, there do seem to be rather more localized effects attendant on such grafts or excisions. Addition of extra cortical material from the future brain region of one embryo to the same site in a second embryo results in slight abnormalities in the brain region [6]. One rather remarkable example of this effect can be seen in figure 6, where duplication of much of the brain structure has occurred.

Grafts of cortex taken from outside the grey crescent region, placed in the crescent of uncleaved fertilized eggs, have the effect of leaving a small island of cells that do not participate in gastrulation. This effect may indicate that the activating properties of the crescent are split into two partially separate regions. The cortex is also concerned with cell division mechanisms. Grafts of cortex from an unfertilized egg were found to block cleavage, even after it has started, in a fertilized one [6], and a disparity in developmental age between graft and hosts using grafts of cortex, produced an effect on the rate of division in the recipient cell.

These results indicate that the cortex carries a remarkable amount of the information required for building an amphibian embryo. The cortex provides a large amount of the spatial information required to determine where each part of the embryo forms, 'mapping it out', as it were. The formation of the dorsal lip and the consequent induction, which leads to visible cellular differentiation, are directly dependent on the grey crescent cortex. The mechanism of cell division and the control of cell movement appear to be related in part to cortical properties.

The circumstantial evidence derived from centrifugation and ligaturing experiments leads to equivalent conclusions about the action of cortical factors in mollusc embryos [2], insect embryos [13], and in echinoderms, where the cortex appears to be composed of no more than the plasmalemma [14].

The structure of the cortex

Unfortunately we are still very ignorant of the structure and composition of the cortex, even in any single species. Despite the widespread group of morphogenetic properties associated with the cortex, it is not clear whether there is any standard cortical structure common to all organisms. The amphibian cortex, unlike that of the echinoderms just mentioned, is comparatively massive. H. Wartenberg and W. Schmidt [15] made electron micrographs of the cortex of the newt, *Triturus alpestris* and of the frog *Rana temporaria* and found that the cortex consisted of a clear cytoplasm layer, containing a few vesicular elements, and an overlying plasmalemma. M. Kidd and I made electron micrographs of the isolated cortex from *X. laevis* eggs, which confirmed this structure and showed that the graft was about 2000 Å thick (figure 7). The amphibian cortex can be shown by optical means to contain a considerable degree of molecular orientation, molecules being lined up with their long axes parallel to the surface. In mollusca, the cortex appears to be composed of a plasmalemma alone, as in echinoderms [2]. For technical reasons it is possible to demonstrate cortical properties in the protozoa only by using grafts of considerable thickness. In all organisms, however, the plasmalemma appears as a component of the structure and is often apparently the only component. It may turn out that it is the seat of cortical properties in all animals. As development proceeds in amphibia, the cortex appears to thin, and after gastrulation there is little more left than the plasmalemma. Whether the cortical properties are contained in the plasmalemma and either act or lie quiescent during the remainder of the animal's life, or whether they are lost as the cortex thins, is uncertain.

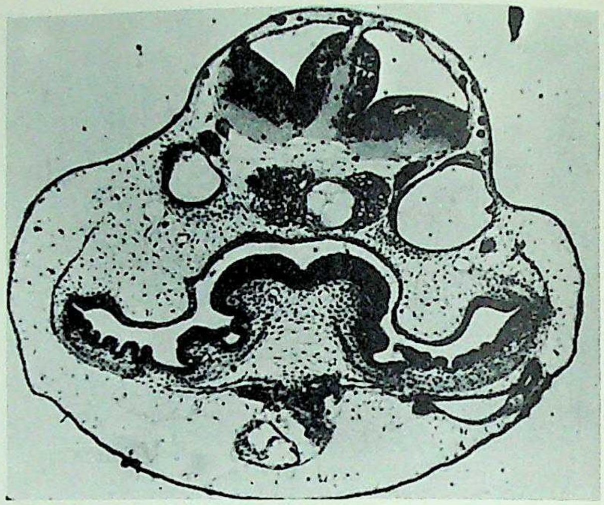

Figure 6 Section through hindbrain region of embryo which had received grafts of additional cortex in future brain region. Note doubling of brain structure (× 52). Celestin blue and eosin.

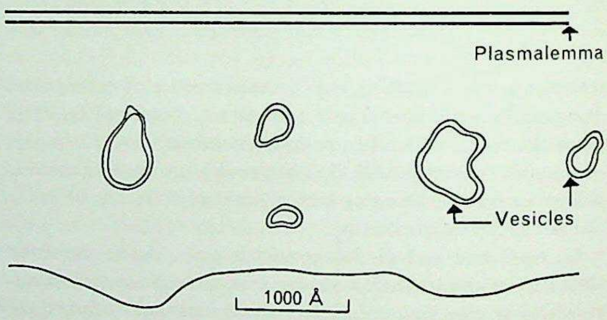

Figure 7 Idealized diagram prepared from electron micrographs of structure of amphibian cortex.

The cortex of *Xenopus laevis* embryos is free from nucleic acids. Its resistance to pancreatic ribonuclease or to deoxyribonuclease, which have no effect on its inductive properties, suggests that nucleic acids are not involved in carrying the instructions that the cortex bears. The reaction of molluscan embryos to various ionic species suggests, according to Raven [2], that a phosphate colloid is involved in the cortical control of embryogenesis. This might be of lipoprotein or phospholipid. Similar ionic effects are known for amphibian embryos. The general trend of this biochemical type of research appears to be towards the identification of the lipoprotein plasmalemma as the structure which is active in carrying the cortical information, but very much more research is needed.

The molluscan cortex is very resistant to centrifugation (2); extreme accelerations, > 100 000 *g*, however do deform the cortical structure to a certain extent. In *X. laevis* the cortex is much less resistant to intense centrifugation, and surface viscosity measurements indicate [16] that the cortex in this animal has bulk properties comparable to a middle bituminous pitch. J. M. Mitchison and M. M. Swann [17] measured Young's modulus for the sea urchin cortex, and their results indicate that it has mechanical properties roughly similar to those of the amphibian embryo. The cortex of amphibian embryos has non-Newtonian flow properties [16]. As Mitchison and Swann suggest, these mechanical properties are probably involved in the control of cleavage. It is hoped that further rheological investigation will throw light on the structure of the cortex.

How cortical factors function

Raven [2] and Fauré-Fremiet [12] have suggested that the precise nature of the molecular construction of the cortex varies spatially over the whole of the molluscan embryo or protozoon respectively, so that each future organ is specified by a particular type of cortical structure. Since the cortex is either in or very close to the cell surface, it is possible that the cortex directly controls the development of the specific surface properties of each cell type. Indeed some suggestive evidence for amphibia in favour of this view has already been mentioned. Obviously it has additional functions to perform in amphibia, and these functions require mechanisms of which we have at present no knowledge. Raven [2] suggests that, in mollusca, the cortex controls the localization of various biochemically differentiated types of cytoplasm shortly after fertilization, and that these in turn perform the inductions and differentiations necessary to produce the various cell types in their correct positions. In insects, the cortex is much more obviously directly involved with the nuclei than in other groups. G. Krause and K. Sander [13] have reviewed the evidence that suggests that the cortex is involved with the activation of the nuclei into their varying roles in differentiation and with the remarkable chromosomal eliminations that occur in many of the embryonic nuclei in certain insect species. It is still not clear how the cortex in protozoa is able to line up and orient the complex ciliary and pigment bands [12]. Obviously, the cortical interactions pose some fascinating biophysical problems.

The egg in most, if not all, metazoons appears to be provided with three systems for the control and specification of the structures that ultimately appear in the adult animal. These are nuclear genes, the cortical factors, and any other cytoplasmic components. Many experiments suggest that the third system is comparatively unimportant in determining the course of embryonic development. In amphibia it has been shown that the genes are very active after gastrulation, but there is little sign of their action before this. However a large amount of fundamental construction of the embryo occurs during pregastrular and gastrular periods, and a considerable portion of this appears to be under cortical control.

The origin of the cortical factors

How are we to integrate the information about the cortical control of embryogenesis with the concept of genetic control of the organism? There are three views of the origin of the cortical structure. The first is that the cortex is synthesized under gene control during egg formation: in such a case the cortex could be regarded as containing one or more of the repressor agents postulated by F. Jacob and J. Monod [18]. A second view is that the cortical pattern is imprinted on the egg from outside during its formation. Raven has described [19] a pattern of various types of cell that surround the developing egg in the ovary. Even if this pattern of cells is involved in the formation of the cortical pattern and is not a consequence of the preexistence of a cortical pattern, there remains the problem of what mechanism controls the arrangement of the cells. The third point of view is that the cortical pattern is self-replicating. There is strong evidence that this is so in the protozoa.

Could a similar mechanism operate in amphibia? Since the cell surface is divided between the two daughter cells when division occurs, and as the grey crescent ultimately gives rise to the sex cells, two of the basic requirements for a self-replicating system exist. These are that the grey crescent, which it is essential to reproduce, is able to get into the line of cells which leads to the germ cells; and that the cortex shall not be lost during mitotic division. I have been testing for the occurrence of cortical self-replication in *X. laevis*. Small defects have been made in the cortex of fertilized eggs in the grey crescent region. The eggs have been raised and the animals are beginning to attain maturity. They are not noticeably different in external appearance from control animals and their sex ratio is normal. A fairly complex system of breeding is in progress to test whether self-replication of cortical factors can happen. If it is found that the eggs laid by these experimental animals have cortices which are in some manner defective, then there will be strong evidence for cortical self-replication. At present the incomplete results suggest that replication does indeed happen. However it is unclear whether this replication happens because the cortex specifies the genes to build a new cortex when egg formation occurs, or because the cortex carries its own independent replicating mechanism. The finding that fertilization of eggs from operated animals by sperm from control males does not correct their defects, and that the sperm from experimental males can fertilize normal eggs, suggests that the sperm makes no significant contribution to the cortex.

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Neural mechanisms in transfer of training

J. deC. Downer

When an organism has learned a new response by training on only one side of the body, it can perform the same type of response, without additional training, when using sense organs or muscle groups belonging to the other side of the body. This ability is known as transfer of training. The study of this phenomenon has taught us much about the memory trace.

The first extensive study of transfer of training occurred in 1844, when E. H. Weber [19] noted that children who had been trained to write with one hand were able to produce good mirror-writing with the other hand without additional training. Since that time many studies have been carried out to see if the transferred behaviour is identical with the original; to see if the transfer is partial or complete; and to see if it applies equally well to both perceptual and sensorimotor learning. These studies have shown consistently that in learning a relatively complex sensorimotor task, practice restricted to one side of the body greatly facilitates performance on the other side of the body, but that the performance on the untrained side is usually less efficient than that of the trained side. With simple perceptual learning tasks, on the other hand, transfer is usually complete and the performance appears to be identical with the original.

This last observation is of such commonplace experience in everyday life that it seems hardly necessary to subject it to experimental verification. If an individual covers one eye and observes a novel stimulus with the other eye, there will be, of course, immediate recognition of the stimulus when the formerly covered eye is used alone. Obvious though this phenomenon may seem, it has many interesting and complicated neurological implications.

In all neuropsychological research on learning it is generally assumed that, when an organism acquires a new mode of response based on experience, some change, of as yet unknown nature, takes place in its central nervous system. This change is, according to the circumstances, of either a transitory or enduring nature. If it endures, the change is the basis for the permanence of recognition, retention, and recall—the behavioural synonyms for memory. This assumption has particular relevance to the problem of transfer of training. In most instances, the larger proportion of each sensory system innervating one side of the body projects to the contralateral cerebral hemisphere. This arrangement might lead one to suppose that when training has been restricted to one side of the body, the memory trace would be formed predominantly in the contralateral cerebral hemisphere. The observation that the organism exhibits transfer to the opposite side of the body raises the question as to whether or not a similar memory trace was established in the ipsilateral cerebral hemisphere during the original learning process. If this is so, then by what route did this hemisphere receive its information? Three possibilities may be considered:

(1) While unilateral training is under way, the memory trace is being formed in the contralateral cerebral hemisphere via the crossed nerve fibre system. As this process is going on, a similar memory trace is being formed in the ipsilateral cerebral hemisphere via the smaller uncrossed part of the nerve fibre system.

(2) While the memory trace is being formed in the contralateral cerebral hemisphere, a similar trace is being formed in the ipsilateral hemisphere, not via direct neural connections with the periphery but through nerve fibres originating in the 'trained' hemisphere and terminating in the 'untrained' hemisphere.

(3) Finally, these two mechanisms may be considered as operating together. That is, the uncrossed nerve fibre system and the nerve-fibre system connecting both cerebral hemispheres together may act, *pari passu*, as alternate or dual routes for the development of the memory trace in the ipsilateral hemisphere (figure 1).

Utilization of the crossed nerve-fibre system

The first possibility has been extensively studied, particularly with respect to the visual system. It has been demonstrated in cats [12], monkeys [5, 16], and apes [3] that transfer of monocularly learned visual discrimination habits is immediate and complete. One explanation for this lies in the unique arrangement of optic nerves and tracts in animals possessing well-developed binocular vision. In monkeys, for example, it is estimated that about 55 per cent of the optic nerve fibres (those arising from the medial half of each eye) cross in the optic chiasma and continue by way of the contralateral optic tract to end in the dorsolateral geniculate nucleus, from which other nerve fibres arise and continue on to the visual area of the cerebral cortex (figure 1). The remaining 45 per cent of optic nerve fibres (arising from the lateral half of each eye) do not cross in the optic chiasma and have their central representation in the ipsilateral visual cortex. There are no known interconnections between the two dorsolateral geniculate nuclei. It can be seen from figure 1 that the medial half of each eye projects to its contralateral cerebral hemisphere while the lateral half of each eye projects to its ipsilateral cerebral hemisphere. It follows that if one eye is stimulated a response will be produced in the visual cortical areas of both cerebral hemispheres, leading presumably to the development of similar visual memory traces in each and thereby producing what appears to be transfer of visual information.

In an attempt to circumvent this particular anatomical arrangement of the visual system, transfer of visual discrimination habits was studied in teleost fishes [15]. These animals have the advantage for this type of investigation of possessing a completely crossed visual system. Should transfer occur, it could not be due to a direct bilateral midbrain response arising from stimulation of one eye. Transfer occurred in all instances, and it was concluded that transfer was mediated by the large fibre system that joins the two halves of the brain together [9]. More recently, the optic chiasma has been sectioned in the medial plane in both cats [10] and monkeys [4], thereby destroying

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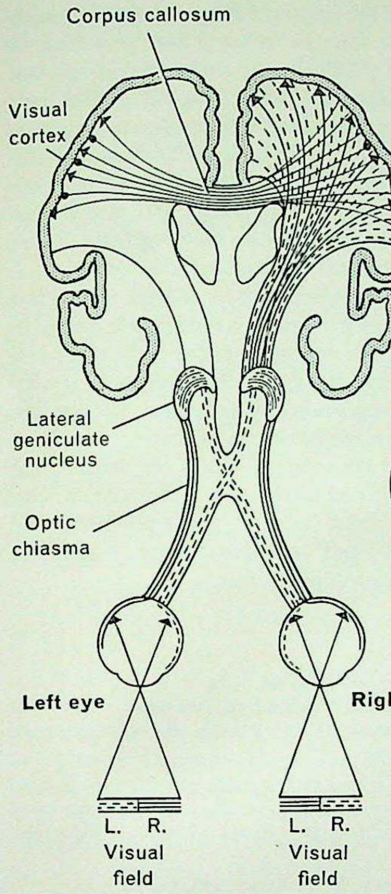
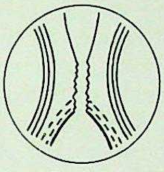
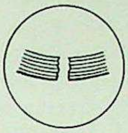


Figure 1



Optic chiasma sectioned

Figure 2



Corpus callosum sectioned

Figure 3

all crossed optic fibres from the eyes and limiting the afferent visual connections from each eye to its ipsilateral half of the brain (see figure 2). Each animal was trained on a number of visual discrimination problems with one of its eyes covered. After learning these tasks, the open eye was covered and the formerly covered eye was opened. When tested on the same problems they all showed perfect retention of the discrimination habit. These studies show that transfer of visual discrimination habits is not solely dependent upon bilateral afferent connections from either eye, but that the visual information must be transmitted from one half of the brain to the other half through bands of nerve fibres originating in one side and terminating in the other side.

Direct communication between cerebral hemispheres

The function of these bands, or commissures as they are named, has for a long time been unknown. Indeed, an eminent neurologist once stated, facetiously perhaps, that their only function was to transmit epileptic activity from one half of the brain to the other. A number of these commissures may be implicated in the transfer of visual memory: the posterior commissure, joining subcortical structures which are in part concerned with ocular motility and reflexes, the hippocampal commissure, which connects the phylogenetically 'older' halves of the brain. The anterior commissure, which has a very small neocortical component, connecting part of the temporal neo-cortex across the midline. This may be of some importance, because the temporal neo-cortex has been implicated in visual learning and memory. Finally, there is the massive corpus callosum (see figure 1). This would seem to be a very likely pathway for transfer of training since it is made up exclusively of axons arising from cortical cells that join areas of the neo-cortex of one hemisphere to homologous areas of the other side. That is, if stimulation of a sense organ produces a response in a cortical area of one hemisphere, information may then be transmitted to the homologous area of the other hemisphere via the corpus callosum.

If transfer is effected solely by the corpus callosum, cutting this structure in the midline should prevent further transfer from taking place (figure 3). The first experimental observation that seemed to support this was reported by K. Bykov [2]. He trained dogs to raise their left forelegs in response to a tactile stimulus delivered to the right side of their bodies. This conditioned response disappeared following surgical sectioning of the corpus callosum. Since that time, many reports have appeared describing partial or complete transection of the corpus callosum in man and in experimental animals. In man, the corpus callosum has been sectioned in an attempt to prevent the spread of excessive neural excitation from one hemisphere to the other during epileptiform seizures [1]. It was reported that following such procedures there were no signs of language weakness (aphasia), impairment of voluntary movement (apraxia), or of perceptual ability (agnosia). Nor were there any observable changes in personality, memory, or the individuals' ability to perform complex motor movements requiring the co-ordinated use of both hands. Furthermore, in a review of the literature covering 123 cases in which congenital absence of the corpus callosum was anatomically proved, it was concluded that, where there was no other neurological involvement, mere absence of the corpus callosum did not produce any observable symptoms [13]. Finally, transfer of monocularly learned visual discrimination habits in man [14] and monkeys [5] was found not to be affected by transection of the corpus callosum.

The evidence so far presented suggests that transfer of visual memory is not solely dependent upon the corpus callosum. There is, however, some recent evidence describing the loss of intermanual transfer in cats [17], and monkeys [6, 7] following division of the corpus callosum. In these experiments, the animals were trained to discriminate between various shapes by touch alone and using only one forelimb. When tested on their ability to make the same discrimination using the opposite forelimb, transfer occurred. When trained on new problems following division of the corpus callosum, some monkeys transferred while others did not. In cats, intermanual transfer failed.

Combination of routes

The third possibility listed above remains to be considered. The crossed nerve fibres and the cerebral commissural system may both be involved in transfer of training. If one route is destroyed, transfer might be mediated by the other. For example, if the optic chiasma is divided in the midline, transfer of visual discrimination habits might be mediated by the commissures. If the commissures alone have been divided, transfer might be mediated by the crossed and uncrossed optic nerve fibres. If this is correct, transfer should not occur in an animal in which all these structures have been divided. This hypothesis was first tested in cats [11], and later in monkeys [4, 16]. Following division of the optic chiasma, corpus callosum, anterior commissure, and hippocampal commissure, animals were trained monocularly on a variety of visual pattern problems. After learning these tasks, they were confronted with the same problems but using the opposite or 'untrained' eye, and were tested to see whether or not they would still continue choosing the appropriate stimuli. In all instances in which the surgical lesions had been complete, the animals acted as if confronted by new stimuli; there had been no transfer of the learning from the 'trained' hemisphere to the 'untrained' one. The independence of the two halves of the brain was so complete that it was possible to train each half of the brain on diametrically opposite stimuli without stimulus conflict or interference. With one of its eyes open, the animal could be trained that a cross was rewarding, and that a circle was unrewarding. When the mask was shifted to its opposite eye, the animal could be trained that the cross was now unrewarding and that the circle was rewarding. Upon learning these discrimination tasks the animal would choose either the cross or the circle depending upon which eye it was permitted to use. In effect, the animals behaved as if, with respect to pattern vision, they had two completely independent brains.

Experimental value of technique

Apart from the information gained about the role of the cerebral commissures and optic chiasma in transfer of visual memory, these experiments have revealed a potentially useful way for investigating the relationship between the brain and behaviour. It seems to be well established, in experimental animals, that bilateral brain lesions must be produced in order to bring about defects in learning and perceptual behaviour. Each cerebral hemisphere appears to be equal to the other with respect to these functions. Sectioning the cerebral commissures and optic chiasma in the midline and closing one eye will restrict the visual input to one hemisphere. Any lesion placed in the cerebral hemisphere receiving the visual input should be functionally comparable, with respect to vision, to symmetrical bilateral lesions in the otherwise normal animal. Furthermore, this procedure would have the advantage of permitting repeated control and experimental observations to be carried out in the same animal. For example, in each new learning situation, the animal can be trained using its intact cerebral hemisphere (by closing the eye projecting to the damaged side), then trained on the same problem when using the damaged side (by opening the eye projecting to the damaged side and closing the other eye).

This procedure can be carried out a considerable number of times, and valid comparisons in visual learning made between the normal and brain-damaged sides of the same animal. Preliminary observations have tended to support these ideas. In the monkey, unilateral removal of the frontal pole of the cerebral cortex and transection of the commissures was found to produce many of the signs usually associated with bilateral frontal pole removals [8]. When the visual input was restricted to the damaged side, the animal showed much more difficulty, by comparison with normal animals, in making a correct visual choice if the interval between the presentation of the stimulus and the time in which it was permitted to respond was increased. Difficulty in such delayed-reaction behaviour is usually associated with bilateral frontal pole damage. Similar observations have been made on emotional behaviour [5, 18]. Bilateral removal of the cellular mass known as the amygdala, converts the normally wild and ferocious rhesus monkey into an extremely placid and docile one. Unilateral removal of the amygdala by itself has little, if any, effect. However, if unilateral removal of the amygdala is carried out in the monkey subsequent to midline transection of all commissures and optic chiasma, a remarkable change in behaviour occurs. If the eye projecting to the undamaged side of the brain is used alone, the animal behaves in its usually aggressive way at the appearance of onlookers. Closing this eye and opening the one projecting to the side from which the amygdala has been removed, produces an animal that appears to be quite docile and tame to visual stimulation. One can in effect, 'remove' and 'replace' the amygdalae, and thereby change the animals' emotional state, merely by opening and closing the appropriate eyes.

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The form and duplication of DNA

John Cairns

Inherited information is contained in the molecules of deoxyribonucleic acid (DNA) that are handed down from one generation to the next. These giant molecules are so large and fragile that they cannot be subjected to ordinary biophysical techniques. This article describes techniques for looking at them, and what has been learnt about their form, size, and manner of duplication.

In the past few years there has been a spectacular advance in our understanding of the mechanisms that decree and control the functioning of living systems. The origin of this advance was undoubtedly the discovery that the nucleic acids, in particular deoxyribonucleic acid (DNA), serve as the repository of genetic information [1, 2]. The inherited characters of each living thing can be seen in terms of the set of chemical reactions that its life involves, the set of structures it can elaborate, and the way in which these unfold during the changing life of a complex animal. All these are now known to be the product of the genetic information contained within the DNA molecules that are handed down and faithfully copied from one generation to the next.

The second stage of the advance was ushered in with the elucidation of the structure of DNA [3, 4, 5]. This has already been described in ENDEAVOUR [6], and so only the briefest summary is necessary here. The molecule consists of two phosphate-deoxyribose chains wound spirally around a common axis; attached to each deoxyribose is a purine base (either adenine or guanine) or a pyrimidine base (either thymine or cytosine), and the two chains are held together by the hydrogen bonds that can be formed between the two purine–pyrimidine base pairs, adenine–thymine (A–T) and guanine–cytosine (G–C). J. D. Watson and F. H. C. Crick [3] suggested that the information in a DNA molecule consists of the precise sequence of the base pairs; thus the genetic message is written with a four-letter alphabet (A–T, T–A, G–C, and C–G). Further, they pointed out that since the base pairs are limited to A–T and G–C, the sequence of bases in one chain absolutely specifies the complementary sequence in the other chain. Thus, A in one chain implies T in the other, and so on. The precise duplication of DNA is essential if the molecule is to act as a safe repository of genetic information. This they suggested would be accomplished if the two chains were to separate and then each act as the template on which new complementary chains were formed. In this way the molecule would provide one chain for each of its two daughter molecules, and these would prove to be a 'hybrid' of one old parental chain and one newly synthesized chain. Their hypothesis has received ample confirmation in the intervening years. It is shown diagrammatically in figure 1.

This article describes recent work on the organization and replication of the DNA of different organisms, from the simplest viruses to bacteria and animal cells. We will not have space to discuss the recent exciting advances in our understanding of the processes that translate the base sequence of DNA into the amino-acid sequence in proteins—that is, translates information into action. Suffice it that genetic information is indeed in the sequence of bases in DNA, that these four bases (A, T, G, and C) constitute a four-letter alphabet, and that with this alphabet the genetic message is written in words of three letters.

Confirmation of the Watson-Crick model of DNA replication

As we have said, Watson and Crick stated that each DNA molecule contains one chain derived from the parent molecule and one new complementary chain. This method of replication has been called 'semi-conservative' [7], as the individual chains are conserved from one generation to the next, but the association of two chains is not.

DNA replication has been shown to be semi-conservative for a wide range of living systems. The experiments have depended on marking in some way the DNA made after the start of the experiment. Thus, bacteria may be uniformly labelled with the heavy isotope ^{15}N so that their DNA shows a detectable increase in density. After one generation in ^{14}N-containing medium (during which time the total quantity of DNA doubles), all their DNA is found to have become a hybrid of ^{15}N and ^{14}N chains, of intermediate density; after another generation and further doubling of the DNA, half the DNA is still an ^{15}N–^{14}N hybrid—showing that the ^{15}N chains are conserved—and half is pure ^{14}N DNA of, therefore, the normal density [8]. This type of experiment is shown diagrammatically in figure 2. It has been given in some detail as it sets the stage for a later section dealing specifically with bacterial DNA.

DNA and genetic information

The information housed in DNA not only determines the nature and properties of all proteins made, and hence the nature of all the products of enzyme action, but also all the systems of control. Thus the bacterial chromosome has been

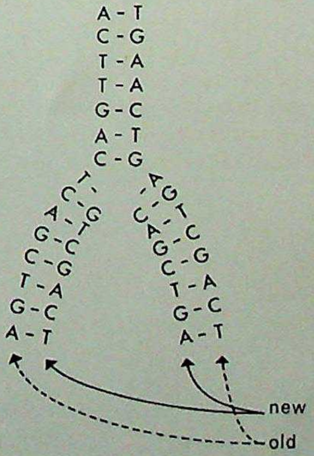

Figure 1 A diagrammatic representation of the scheme of base pairing and replication proposed for DNA by Watson and Crick. The four bases, adenine, thymine, guanine, and cytosine, are represented by the letters A, T, G, and C. The total length of molecule shown would be about 50 Å (0·005 μ).

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Was born in 1922 and was educated at Oxford University. He spent two years at the Walter and Eliza Hall Institute in Melbourne and has been at the Australian National University since 1955. His research has mostly been in the field of virus multiplication.

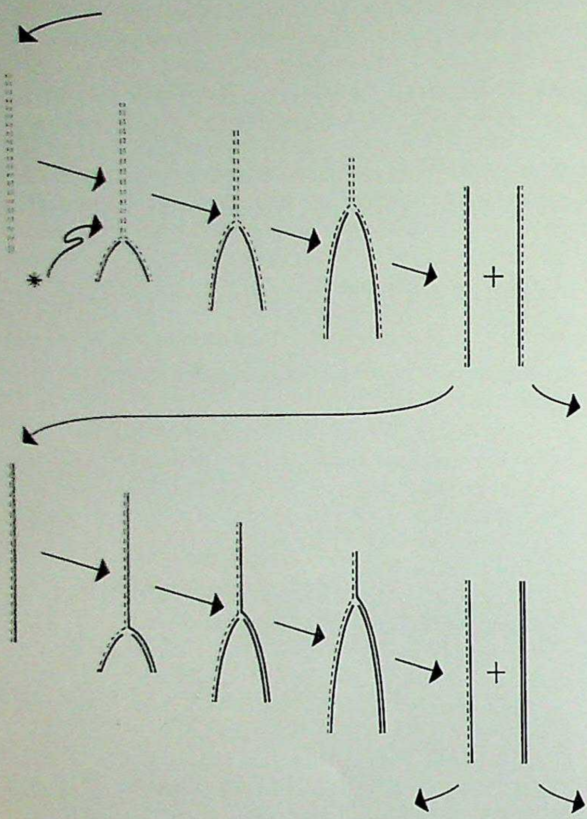

Figure 2 Two rounds in the duplication of DNA. Only half of the family tree is shown for the second generation. The asterisk marks the introduction of some new label (such as ^{14}N or ^{3}H) to mark the chains made from that time on; these are drawn with continuous lines to distinguish them from the old chains.

shown to contain regions concerned solely with switching on and off the executive action of other regions; in turn, these 'operator' genes are controlled by 'regulator' genes. It is the presence of such control mechanisms that converts what might be purposeless or even self-destructive activity into the ordered system we find in every living creature. Further, there is good reason for thinking that the evolution of increasingly complex forms of life has depended upon the elaboration of such control mechanisms, rather than upon a mere increase in biochemical complexity.

The amount of DNA in different organisms varies over a wide range. Taking the genetic language as being made up of words of three letters (three base pairs), viruses contain 2000–50 000 words, bacteria contain 1–2 million words, and each mammalian cell carries with it about 2000 million words. In the remainder of this article we deal with the way viruses, bacteria, and cells package and duplicate this material.

The DNA of viruses

It is proper that this discussion of the organization of DNA start with a section on the DNA of the bacterial virus T2. More work has been done on this variety than on any other, and so more is known about it; also, the molecule is sufficiently large to give many special problems in handling. The techniques involved include most of those used to get round such problems.

Genetic analysis has shown that all the mutable characters of T2 fall in a single linear unbranched linkage group. This suggested that each virus particle might contain a single molecule of DNA. The results of simple chemical analysis gave a fairly precise value for the size of this hypothetical molecule: each virus particle contains about 170 000 base pairs, corresponding to a molecular weight of rather over 100 million. When extracted, the DNA was obviously in very large molecules. However, the standard biophysical techniques for determining molecular weights lack precision when applied to objects of this size and shape. Thus, from the measurement of the sedimentation coefficient of this DNA it was clear only that each virus particle contains a very few molecules that were virtually identical. So the problem became one of determining, by some special unorthodox technique, how many molecules each virus particle has, and then of using this knowledge to calibrate the biophysical technique.

Several methods have by now been used to show that each particle contains one DNA molecule. Most directly, the virus DNA may be labelled by growth in the presence of radioactive phosphorus; each particle will then give rise to multiple electron tracks when embedded in photographic emulsion. By counting the number of such radioactive sources, or 'stars', it was possible to show that on extraction of the DNA, the number of stars remained unchanged. This showed that the total number of DNA molecules was equal to the total number of virus particles [9]. This technique is one form of autoradiography; it can be elaborated further by counting the number of tracks emanating from each star. In this way, one can get a direct measurement of the total number of phosphorus atoms, and thence of the total mass of the labelled molecule [10]. Neither of these methods, however, gives any information about the form of this DNA; it might, for example, be a rod, a circle, or some multi-stranded structure.

The most direct method of inspecting the molecules is, of course, by electron microscopy, and it was in this way that they were shown to have the width, 20 Å, expected for two-stranded DNA [11]. However, the technical difficulties in obtaining a photograph of an entire molecule have not been overcome. This is not surprising when one considers that it must be about 25 000 times as long as it is thick.

In order to measure the molecular length, we have to return to the autoradiography of radioactively labelled DNA in nuclear emulsion, a special photographic emulsion. The radioactive isotope of hydrogen, tritium, emits a very weak electron whose range in nuclear emulsion is usually less than one micron. So the length of DNA molecules may be determined, with a resolution of about a micron, by labelling them with tritium and then covering them with a thin layer of emulsion. Such an autoradiograph of T2 DNA, labelled by the incorporation of ^{3}H-thymine, is shown in figure 3. This picture shows that the molecules are about 50 μ long. This length is about right for a molecular weight of 100 million.

Several other bacterial viruses have been investigated by these various techniques. In every case, they have been shown to contain all their DNA in a single molecule. Perhaps the most startling of this group of viruses is the one called φX 174, which has been shown to contain only one DNA chain, in the form of a circle [12]. However, even this abnormal DNA has been shown to acquire a second complementary chain at the time of replication, so at least its method of duplication appears to be usual.

The DNA of bacteria

In 1946, J. Lederberg and E. L. Tatum demonstrated mating and recombination in the bacterium *Escherichia coli* [13]. Since then, the subject of bacterial genetics has expanded and has

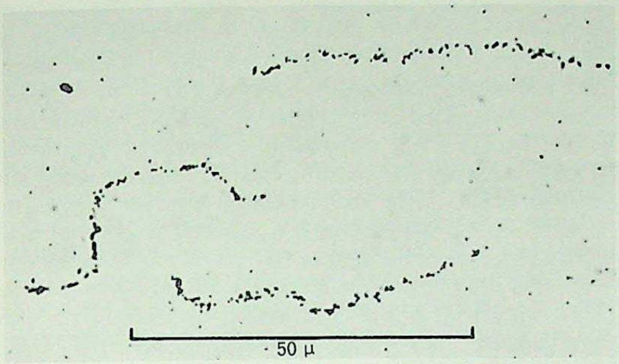

Figure 3 An autoradiograph showing three molecules of T2 bacteriophage DNA, which had been labelled with ^{3}H-thymine and extracted from the virus particles with phenol.

become one of the most important in the entire field of genetics. It has been pursued, firstly with an eye to understanding the peculiarities of the mating process used by bacteria, and also because it is in this system that the manner of gene action is most easily dissected. The knowledge of genetic control mechanisms mentioned earlier, for example, came from the study of bacterial genetics. Here, however, we need only say that the genetic material of certain bacteria has been shown to comprise a single linkage group and that this linkage group appears, in genetic analysis at least, to be in the form of a circle [14].

One of the impressive features of the DNA molecules isolated from the larger bacterial viruses is their great fragility. As one might expect, this fragility is most marked for the largest molecules: these are easily broken by shear and turbulence, particularly when their concentration is low. The bacterial 'nucleus' contains much more DNA than does the largest virus, and hence, if the DNA is a single molecule, it is going to be very fragile. So, in trying to demonstrate that here too there is only a single DNA molecule, methods had to be employed that did not demand moving the DNA once it had been extracted. There are, at the moment, only two such methods, electron microscopy and autoradiography.

One other fact made this investigation of the form of bacterial DNA particularly interesting. Before any cell can divide, it naturally has to duplicate its DNA, so that each daughter cell can receive the full set of genetic instructions. In animal cells, this stage of DNA synthesis occupies only a small part of the time spent between successive cell divisions; at any moment, most cells are not making DNA. However, rapidly multiplying bacteria make DNA throughout the whole division cycle; no sooner has one round of duplication been completed than the next round starts. If therefore we find that the genetic material of bacteria, like that of viruses, is contained in a single molecule, this molecule should usually have been caught at some stage in its process of replication. We are, in short, looking not only for very large molecules but also, specifically, for molecules that are undergoing duplication.

The first good pictures of extracted bacterial DNA were obtained by electron microscopy [15], and one of these is shown in figure 4. In this picture we see, pouring out of the broken bacterium, a tangled mass of DNA, the total length of which must be about half a millimetre, perhaps half the calculated total length of DNA present. No obvious branches can be seen, and this agrees with the absence of branches in the genetic map. More important, no free ends can be seen, suggesting that the bacterial nucleus may indeed contain only one molecule of DNA.

The existence of this single molecule has been demonstrated

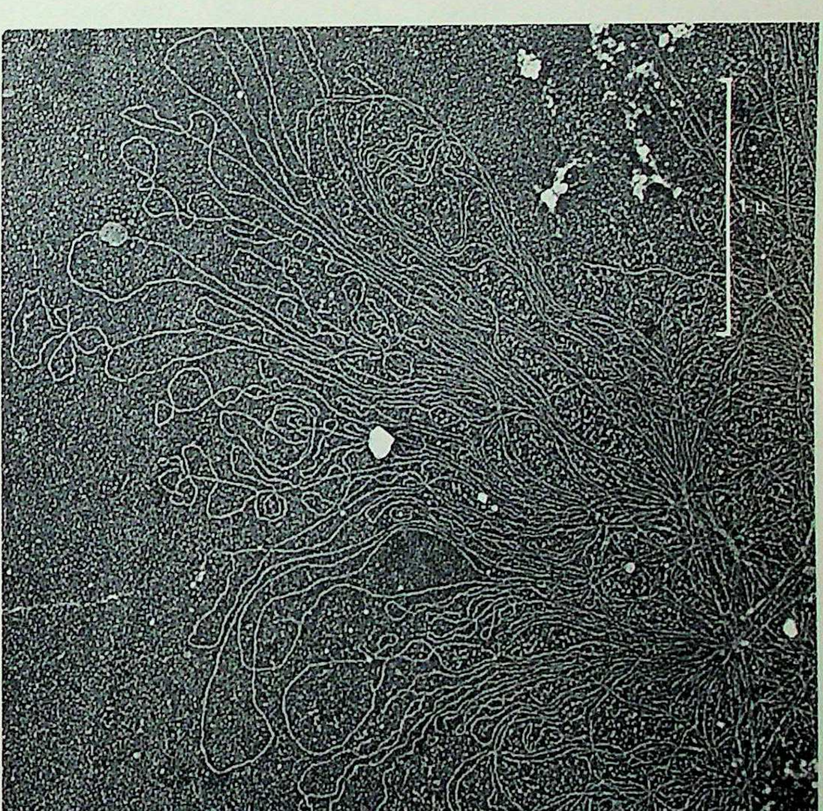

Figure 4 An electron micrograph of the deoxyribonucleoprotein liberated from the bacterium *M. lysodeikticus* when it burst at an air–water interface [15].

by autoradiography. We labelled bacterial DNA by growing bacteria in the presence of the DNA precursor, ^{3}H-thymidine, and extracted it by very gentle methods that avoided, as far as possible, turbulence and shear. Since therefore the only forces left to unravel the DNA were diffusion and convection currents, it was not surprising to find that the DNA of most bacteria had stayed inextricably tangled, presumably as in figure 4. However, occasionally the tangle had come undone, and we concentrated on these instances in the hope that the DNA that they show is typical in other respects. Sometimes the DNA is found complete and unbroken (figure 5), and then it is seen to be in the form of a circle. This agrees with the results of genetic experiments. At other times, and much more commonly, the circle is broken (figures 6 and 7). Although autoradiography cannot capture every minor meander in these molecules, they are obviously about a millimetre long—that is, they have a molecular weight of about 2000 million. As this is roughly the total DNA content of the bacterial nucleus (when the observed value is corrected for the excess due to continuous synthesis), it seems that we do have here the entire bacterial 'chromosome'.

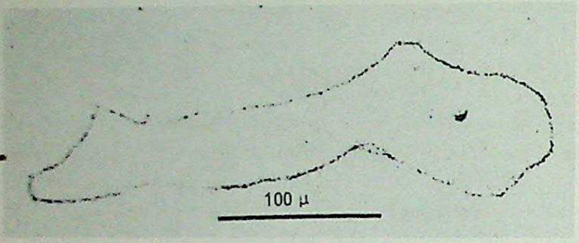

Figure 5 The DNA of the bacterium *E. coli*, labelled with ^{3}H-thymidine and extracted by digestion with the enzyme lysozyme. Some regions of the molecule are not completely extended.

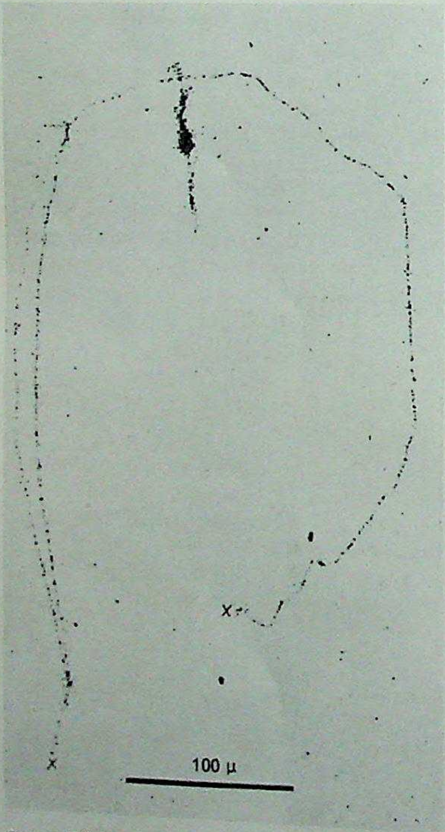

Figure 7 (above) *E. coli* DNA. As for figure 6. The position of the break, that converted the circle into a rod, is marked X—X. One completely tangled molecule is also present.

Figure 6 (left) *E. coli* DNA labelled with ^{3}H-thymidine and extracted with the detergent, sodium lauryl sulphate. The upper end of the molecule has not untangled completely. The scale shows 100 μ. (This and figure 7 are reproduced by permission of Academic Press Inc.)

Part of the object of looking at bacterial DNA was to see DNA molecules in the process of duplication. For this reason the bacteria were labelled for slightly less than two division cycles—that is, for slightly less than two rounds of DNA duplication. The kind of thing we hoped to see is shown in the second half of figure 2. Thus, if duplication of the molecule starts at one end, or at only one point in the circle, the main body of each molecule should be labelled in only one strand and should fork at some point into two limbs; one of these limbs should be labelled in both strands, and therefore have twice the grain density, and the other should be labelled in only one strand. As figures 6 and 7 show, that is exactly what was found. Figure 5 shows the replicating fork less clearly, either because the molecule had not untangled completely or because, in this case, no steps had been taken to remove any protein bound to the DNA. Since, however, the molecule is in the form of a circle, the terminal ends of the fork are usually found joined together. And a separate experiment, measuring the rate of DNA synthesis, was necessary to show that, in fact, the fork travels in only one direction. These findings are summarized in figure 8.

The DNA of plants and animals

The techniques for handling large molecules of unbroken DNA have been developed recently, but there have so far been no reports on their application to higher organisms. Though the DNA of more complex cells is partitioned among several chromosomes, the total amount of DNA in each of these

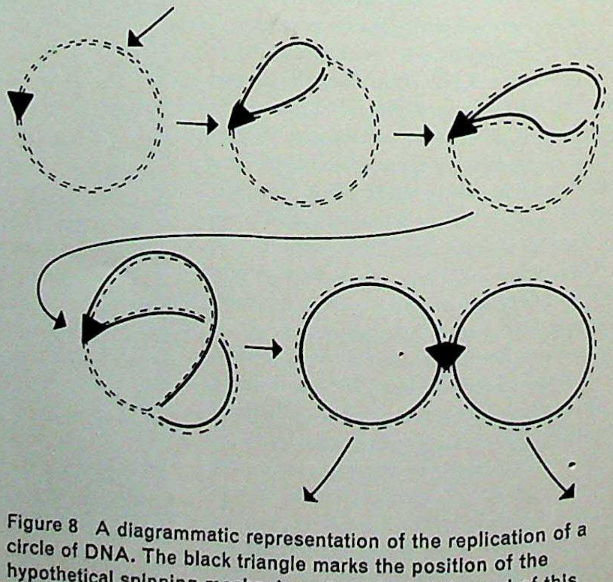

Figure 8 A diagrammatic representation of the replication of a circle of DNA. The black triangle marks the position of the hypothetical spinning mechanism discussed at the end of this article.

chromosomes is usually far greater than the amount in a bacterium; each human chromosome, for example, contains on the average about two centimetres of DNA. Considerable technical skill will be needed to display such molecules, if they exist. In the meantime, there are two rather tenuous reasons for thinking that they will be found.

Though the DNA of large chromosomes has not been looked at directly, one may nevertheless get some idea of its form from its behaviour within the chromosome at the time of duplication. If a marker, such as tritiated thymidine, is fed for a short time during the period of DNA synthesis in a plant cell, both the daughter chromatids[1] are found to be labelled at the time of cell division, when they become visible; however, after a further round of duplication these two chromosomes are each found to have produced one labelled and one unlabelled chromatid [16]. This is just what would be expected if each of these chromosomes contains a single molecule: a short period of radioactive labelling makes two molecules each of which is 'hot', or partly hot, in one, new, strand and 'cold' in the other old strand; each of these, if allowed to duplicate in the absence of label, adds a new cold strand to each of the strands it has, and so gives rise to one 'hot–cold' molecule and one 'cold–cold' molecule. One has to admit, however, that these results do not compel one to believe that each chromosome contains only one molecule for, strictly, they tell one about the segregation of the material present and not about the number of strands present; many molecules could be so organized that their chains segregated in this particular way.

The second argument is more tenuous still, though it is of some interest in its own right. The enzyme responsible for the duplication of DNA has been isolated and shown to duplicate DNA *in vitro* [17], starting at the end of the molecule and working along from there [18]. We have already seen how the bacterial chromosome is also duplicated by a process that runs from one end to the other. If therefore we take this to be the rule, and assume further that the rate of duplication is the same for all DNA, we can at least check whether the time known to be spent in duplicating one of the larger chromosomes is long enough for a single process to have run the whole length of the DNA present. This calculation is set out in the table. We can see that there is a case for believing in a universal duplication rate, and this, in turn, gives some support for the idea of one molecule for each chromosome. At the same time, it is known that there are chromosomes for which this is not true. For example, the giant chromosomes in the salivary cells of *Diptera* undergo repeated rounds of DNA synthesis without separating the products, so they certainly contain more than one molecule.

Although a lot has been learnt about the form of DNA and the way in which it replicates, there are many outstanding problems left, as well as some problems created where there were none before. Extraordinarily little is known about the forces that compel DNA molecules possessing very similar base sequences to align and then exchange strands. This reaction is at the very heart of genetic recombination. And yet one has no idea how similar molecules identify each other, let alone why, when this has been accomplished, there should be any tendency for cross-over to occur.

Closer to the subject of this article, there are problems to do with the sheer mechanics of DNA replication. The two chains of the molecule, which for simplicity's sake we drew parallel in all the diagrams, are actually wound helically around a common axis, with one complete turn for every ten base pairs. So, for them to come apart, the main body of the molecule must spin one revolution about its own axis for every ten base pairs that are separated. For this reason, the universal duplication rate corresponds to rotation at about 10 000 revolutions a minute. For smaller DNA molecules this is energetically quite feasible [19]. But when the molecule is a millimetre long, one is inclined to look for some additional mechanism, specifically entrusted with the task of spinning the molecule. This mechanism would have to be strong enough to overcome the viscous drag; more notably, it would have to be so arranged that it turned the main body of the molecule in relation to the far end and did not merely turn itself and the whole molecule in relation to the rest of the cell. We see at once a good reason for having the molecule in the form of a circle, for to anchor the spinning mechanism also to the other end of the molecule is the simplest way of ensuring that every rotation undoes the double helix another turn.

	Total DNA content (μ)	Duplication time at 37°C (min)	Duplication rate (μ/min)
T2 bacteriophage	50	1–2	(25–50)
Escherichia coli	1000	30	33
Human chromosome	(~ 20 000)	~ 400	(~ 50)

The values in brackets are those calculated rather than observed directly.

It is proper that the article should end, like this, with an unsubstantiated hypothesis. Even though we know so little, we can at least be sure that some most precise mechanism watches over the preservation and duplication of this, the most important of biological molecules.

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[1] The word 'chromatid' is used here to avoid offending the sensibilities of geneticists. In the present context it has the same meaning as the word chromosome.

Nuclear matter

R. E. Peierls

The study of matter has gone through four stages of refinement. Firstly, it was concerned with matter in bulk; secondly, with atoms as a whole; thirdly, with the outer shells of atoms; and fourthly, with the nucleus. Although these different levels of inquiry pose their own problems, they also have certain affinities. This review emphasizes that the concepts of classical physics, and those developed later to account for phenomena in atomic physics, have their place in interpreting the properties of nuclear matter. To the latter can be ascribed such familiar properties as density, surface tension, and specific heat, and a shell structure analogous with that of atoms.

The list of atomic nuclei that exist in nature or can be produced in the laboratory is extremely long, and still growing; a full account of all their properties would fill many volumes. For any understanding of this bewildering amount of material it is necessary to have some simple description of the general trends, so that the features of specific nuclei can be looked at in perspective.

The most obvious general trend is that the specific quantities for all but the smallest nuclei are similar. In particular, they have the same specific volume—the same volume per particle—and the same binding energy per particle. In other words, the conditions in the interior of a reasonably large nucleus are independent of its size. The state of the nucleons—the physicist's generic term for neutrons and protons—in the interior is called nuclear matter. We may therefore think of nuclei as small amounts of nuclear matter, in the same sense as a raindrop is a small amount of water.

The ideal form of nuclear matter, like that of water, is uniform, but only the interior of a nucleus consists of nuclear matter of this kind. The material near the surface is in a different state. To study nuclear matter in its purest form, we shall therefore look at very large nuclei, in which the surface-to-volume ratio is relatively small.

Nuclei are limited in size because, as they become larger, their electric charge increases, and the mutual repulsion of like charges causes a tendency to fission. Hence nuclei become unstable above a certain size, and the largest nuclei that live long enough to be used for experiments contain some 250 nucleons. This looks like a large number, but it must be remembered that the diameter of a sphere of 250 balls packed closely together is only about six times the diameter of a single ball, and that more than half the balls are in the surface layer. The comparison of actual nuclei with uniform nuclear matter therefore necessarily involves some idealization, and one must not try to learn too much from the picture. Within the proper limits, however, the concept of nuclear matter can be very helpful and informative.

Nuclear matter has all the properties with which we are familiar from other forms of matter. All the familiar quantities—such as density, viscosity, and specific heat—may in principle be defined for the nucleus, though not all of them are of practical interest to the nuclear physicist. In this survey we shall first discuss those properties that have a bearing on nuclear experiments and then discuss the theoretical problems involved in accounting for them.

R. E. Peierls, *C.B.E., F.R.S.*

Was born, in 1907, and educated in Germany, studying under, among others, Sommerfeld, Heisenberg, and Pauli. He came to Britain in 1933, and became Professor of Mathematical Physics at Birmingham in 1937; he has now been appointed Wykeham Professor of Theoretical Physics at Oxford. His main interests are in quantum theory, including solid-state physics, nuclei, and field theory.

Properties of nuclear matter

Density. It has already been mentioned that the nuclear volume is found to be proportional to the mass number, that is, to the number of nucleons contained in the nucleus. The best evidence on nuclear radii comes from the Stanford experiments on the scattering of fast electrons by nuclei [1]. In these experiments, the electrons are fast enough to be deflected only slightly from their initial direction by passage through, or close by, a nucleus, and their de Broglie wavelength is small compared with the dimensions of the nucleus. In these circumstances, the angular distribution gives—to a good approximation and subject to corrections that can be allowed for—a diffraction pattern from which the charge distribution can be determined. The density of protons as a function of distance from the centre can thus be calculated, at least in the case of nuclei that may be regarded as spherical.

It is found that the proton density is uniform over the interior of the nucleus, falling off rapidly at the edge (figure 1, curve a). It is probable that the density has a slight dip at the centre, resulting from the electric repulsion between the protons, which tends to push them out towards the surface (figure 1, curve b). This dip is expected theoretically; it is compatible with the experiments, but is near the limits of the accuracy of the analysis of the data.

There are good reasons for believing that the distribution of neutrons closely follows that of the protons. The curves of figure 1 therefore also represent the distribution of mass. The central, uniform part of the curve represents the conditions in nuclear matter. The actual density of nuclear matter is found to be about $1{\cdot}7 \times 10^{38}$ nucleons/cm^3, or $0{\cdot}17$ nucleons/fe^3, using the nuclear physicist's unit of length (1 fermi (fe) $= 10^{-13}$ cm). This is not exactly the equilibrium density of uniform nuclear matter, because a small drop of any material is under pressure due to the surface tension, although this is, for the nucleus, reduced by the electrostatic repulsion. The correction is not very great, making the density perhaps $0{\cdot}2$/fe^3 ($3{\cdot}3 \times 10^{14}$ g/cm^3).

Energy density [2]. Nuclear binding energies are known rather accurately from the masses (atomic weights) of the

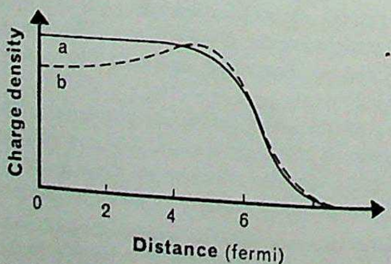

Figure 1 Charge distribution in a heavy nucleus [1].

nuclei, for which Einstein's relation $E=mc^2$ gives directly a measure of energy content. The accuracy can be improved by taking into account experiments on nuclear reactions in which the energy involved in adding one or more nucleons to a nucleus can be determined. Figure 2 shows the binding energy per nucleon of the most stable nuclei as a function of mass number A (number of nucleons). This falls off on the left because of the greater relative importance of the surface energy for the small nuclei. It drops also on the right, because of the electrostatic repulsion of the highly charged heavy nuclei. As a result of this repulsion, the balance between neutrons and protons is also shifted somewhat in favour of the neutrons; the mass number of a heavy nucleus is somewhat more than twice its atomic number. Since the attraction between nucleons is most effective when the numbers of neutrons and protons are equal, this causes a further reduction of the binding energy in heavy nuclei.

All these contributions vary in different ways with the mass number, and they can be isolated by fitting a suitable formula with adjustable parameters to the curve of figure 2. In this way, we find the energy of uniform nuclear matter, disregarding electrostatic forces, to be 15 MeV/nucleon. In other words, the energy density of nuclear matter, taking the energy of free nucleons as reference, is -31 MeV/fe^3 (-5×10^{33} erg/cm^3).

Surface tension. In fitting an empirical formula to the curve of figure 2, we have already used a term representing the surface energy. The coefficient of the relevant term in the formula therefore gives directly the surface energy. The result is about 1·3 MeV/fe^2 ($2{\cdot}1\times10^{20}$ erg/cm^2).

Compressibility. The compressibility of nuclear matter cannot be determined empirically in any simple way. It is, nevertheless, an interesting quantity, since it appears in many calculations relating to nuclear reactions. But as these always involve also other quantities that are not directly observed, they cannot be used for a direct determination of the compressibility.

However, the theoretical value should be fairly reliable, since the theory has to predict the equilibrium density and the energy of equilibrium. A theory which gives these two quantities directly is likely to be good also for deducing the variation of the energy near the equilibrium, which leads directly to the compressibility. The theory of Brueckner and Gammel (see later) gives for the compressibility about 2·7fe^3/MeV or $1{\cdot}7\times10^{-27}$ atmospheres^{-1}. The velocity of sound in nuclear matter should therefore be about 15 per cent of the velocity of light.

Specific heat. If a nucleus is struck by an energetic nucleon, or absorbs a γ-quantum, it may be left in a state in which the excess energy is shared between many degrees of freedom. The motion of the nucleons is then exactly like thermal agitation, and we can apply all the concepts of statistical thermodynamics. If the excitation is high enough to produce emission (evaporation) of nucleons, these will possess only a fraction of the available energy, just as the energy of a water molecule evaporating from a water drop is only a small fraction of the thermal energy of the whole drop.

The emitted nucleons obey, in fact, Maxwell's law of velocity distribution, appropriate to the temperature of the nucleus or, more precisely, to the temperature of the nucleus remaining after the emission, because the cooling resulting from the evaporation of a single nucleon is usually not negligible. By considering the energies of nucleons ejected in such reactions, we can measure the temperature of a nucleus containing a known amount of energy, and so deduce its specific heat.

There was at first some difficulty with this analysis, because the number of ejected nucleons having the whole available energy, or a large fraction of it, was much greater than the Maxwell distribution would predict. However, this was explained as emission occurring before the energy was shared between all available degrees of freedom, that is, before thermal equilibrium was established.

Information about the specific heat has been obtained both from laboratory bombardment, and from observation of cosmic-ray events in which nuclei are struck by particles of extremely high energy.

A second type of experiment relating to the specific heat is the observation of slow-neutron resonances. A slow neutron colliding with a nucleus of mass number A may form a nucleus of mass number $A+1$ in a highly excited state, because the capture of a neutron releases an energy of some 6–8 MeV. In spite of its high excitation, this nucleus may exist for some time, because it is difficult for any one nucleon to pick up enough of the total energy to escape. It therefore has quite sharp energy levels, which show up as resonances, that is, as energies for which the chance of capture of the incident neutron is exceptionally high. This resonance phenomenon makes it possible to count the number of energy levels in a given range of energy; this number is, by the principles of statistical mechanics, closely related to the entropy. We thus find a relation between energy and entropy, from which the specific heat can be derived by thermodynamic arguments.

Strictly speaking, these results relate to the specific heat of finite nuclei, and not to nuclear matter. An exact treatment would require investigating this as a function of the weight of the nucleus, and then deriving the specific heat of nuclear matter in the same way as the energy density was derived from the curve of figure 2. Present data are not extensive enough for such a procedure, but nevertheless they do provide some approximate information about specific heats.

The results show [3] that the specific heat increases with temperature. They are compatible with a law

$$E=\tfrac{1}{2}\gamma T^2$$

for the thermal energy, where the constant γ is of the order of

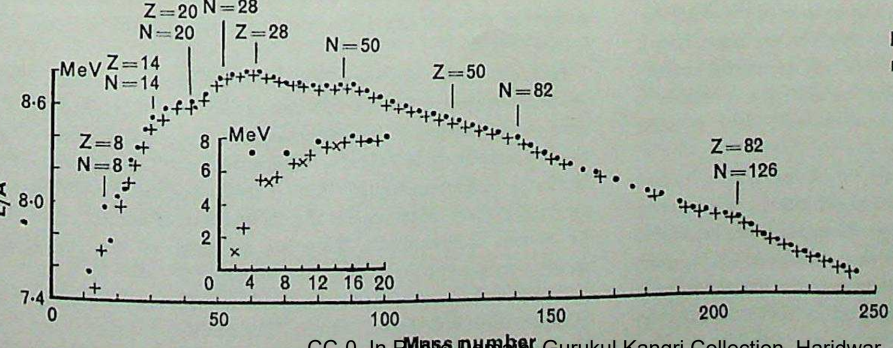

Figure 2 Binding energies of stable nuclei [2].

magnitude $\frac{1}{4}$ MeV^{-1} per nucleon if the temperature is measured in MeV.

This small value indicates that even at a temperature of one MeV per particle, nuclear matter has a specific heat one-twelfth of that required by the equipartition law and is comparable to ordinary matter at very low temperatures.

Theoretical considerations

Reasons for saturation [4]. The properties of nuclear matter present a challenge to the theorist. The first problem is why nuclear matter has a distinct equilibrium density, that is, why, with increasing number of particles, nuclei do not get denser and denser, as is the case with atoms. This depends, of course, on the nature of the forces between nucleons. If all nucleons attracted each other in all circumstances, they would cause the nucleus to contract until each nucleon was within the range of attraction to every other. The fact that this does not happen is attributed to what is called saturation.

In discussing this problem it is important to take account of Pauli's 'exclusion principle', which states that—in quantum theory—no two electrons, and no two nucleons, can ever be in exactly the same state of motion. This principle was first found necessary to explain the structure of atoms. In an atom the first electron moves in the orbit with the lowest energy, the 'K shell'. A second electron may move in the same orbit, since electrons spin about their own axis, and quantum theory allows this spin to have two alternative directions. The Pauli principle allows two electrons in the same orbit spinning in opposite directions, so that the K shell has room for two electrons, and is complete in the helium atom. The next electron has to go into a larger 'L shell', and is therefore less strongly attached to the atom. Lithium, with three electrons, is understandably easier to ionize, and therefore chemically more active, than helium. By considering the successive filling of the shells in this way, one is led to an understanding of the Periodic System of the elements.

This principle appeared at first to be independent of the other laws of quantum theory. Later we learned that it was necessary in order to make the quantum theory of electrons consistent, but the reasoning for this is too deep to be pursued here. The principle applies equally to nucleons, and in order to accommodate many nucleons in a small volume, one has to arrange them in different states of motion, that is, make some of them move with appreciable velocities. Quantitatively, it turns out that the distribution-density of each type of nucleon, spinning in each sense, can at most amount to four such particles in a volume equal to the cube of the de Broglie wavelength of the fastest of them; in other words, sixteen nucleons in all per wavelength cubed. Since the de Broglie wavelength is h/mv (h=Planck's constant, m=mass, v=velocity), higher densities, requiring shorter wavelength, imply greater kinetic energy.

Thus the exclusion principle opposes collapse, but the kinetic energy per particle increases only as the square of the velocity, and therefore as the $\frac{2}{3}$ power of the density. On the other hand, with purely attractive forces the (negative) potential energy per particle increases as the density, until each particle is exposed to the attraction from every other one. Thus, overall, the attraction should dominate.

The reason why ordinary matter, such as water, shows saturation is that two molecules attract each other only at fairly large distances, but the force between them becomes repulsive at close approach, as if the molecules were impenetrable to each other. Nuclear physicists were at first reluctant to postulate a similar short-range repulsion between nucleons, since the attractive forces have only a very short range, about 2 fermis; the idea of an even shorter-range repulsion, which would have to be extremely strong to be effective, seemed far-fetched. Later data from experiments on proton-proton collisions at high-energy have, however, shown evidence for a strong repulsion at distances of about 0·4 fermi, so that nucleons do in fact behave as impenetrable spheres of this diameter.

Another mechanism for saturation is familiar from homopolar molecules. In these, each atom has a limited number of 'valencies' and therefore can interact with only a limited number of partners. Heisenberg postulated an analogous mechanism for nuclear forces. He was led to the idea of 'exchange forces', as a result of which, in each encounter between a neutron and a proton, the two exchange places. Particles cannot easily make sudden changes in their position or their velocity, and therefore exchange forces are effective only between particles which practically coincide in space and move with the same velocity, that is, between particles in identical orbits. But from the Pauli exclusion principle, at most two neutrons and two protons can be in the same orbit, so that by exchange forces each nucleon can interact with only a few others.

Experiments on fast neutron-proton collisions confirmed Heisenberg's conjecture, but they also showed that the exchange forces represented too small a part of the total interaction to ensure saturation. Thus one has to invoke both exchange effects and a short-range repulsion to account for saturation, and we know from direct evidence that both exist.

Theoretical picture. Having identified the essential features of the forces between nucleons, one must next develop a qualitative picture of how they operate in nuclear matter. In ordinary condensed matter, the forces between atoms favour a regular pattern in which each atom is in an equilibrium position, that is, in which the forces due to its neighbours just balance. To distort such a pattern either by altering its density, or by causing a shear, requires a force.

Such a substance is a solid; most ordinary substances become solid at sufficiently low temperatures. The only exception is liquid helium, which remains liquid even at the absolute zero of temperature, unless a high pressure is applied. The reason for this lies in the uncertainty principle of quantum theory, which states that the position and velocity of a particle cannot both be determined accurately. Any experiment that tends to determine the position of a particle must result in a corresponding uncertainty about its velocity. If, therefore, the atoms of a solid were accurately located in their equilibrium positions, quantum theory would require them to have a large random velocity, and hence a high kinetic energy.

The true state of a solid at low temperatures is a compromise between the effect of the forces, which tend to keep the atoms localized, and the kinetic energy which, because of the uncertainty principle, opposes such a localization. The atoms therefore retain, even at zero temperature, a 'zero-point motion', which is greater the lighter the atoms and the weaker the forces.

Helium atoms are very light and the forces between them weak, as is shown by the low temperature of liquefaction; the zero-point motion is intense enough to prevent solidification. Such a substance is called a 'quantum liquid'. Nuclear matter is also a quantum liquid. This is indicated by the absence of any solid-state features in the behaviour of nuclei, and can be shown theoretically from an estimate of the zero-point motion in a hypothetical solid nucleus.

Thus within our practical experience the closest analogue to nuclear matter is liquid helium. The analogy with the common isotope, ^{4}He, is not, however, close, since ^{4}He atoms—unlike electrons or nucleons—do not obey the Pauli exclusion principle. Instead of being reluctant to move in the same path, ^{4}He atoms have a preference for doing so, and this is important in relation to the very interesting behaviour of ordinary liquid helium at low temperatures. The light isotope, ^{3}He, however, does obey the Pauli principle, and is a much better analogue for nuclear matter, allowing, of course, for differences in the nature of the cohesive forces.

The exclusion principle facilitates the theoretical treatment, because it makes the motion of each nucleon largely independent of the detailed behaviour of the others, in spite of the strong forces. We remember that, at high density, all possible states of motion with low energy are already occupied. An encounter between two nucleons cannot therefore result in small changes in their directions of motion, as would happen in such an encounter in free space, since this would take them into states of motion that are already occupied.

Figure 3 represents schematically the possible states of motion of nucleons, with the levels up to E_F, the 'Fermi energy', occupied and the rest vacant. In an encounter between two nucleons in the states labelled b and b', or c and c', the only possible change is to transfer them to states such as a and a', respectively. This always requires a net increase in energy. In the case of b and b', which are just below E_F, this change is not very large, if they end up in states just above E_F, but for lower-lying states like c, c' the required energy is substantial. In other words, most collisions between most pairs of nucleons can disturb their motion only by a substantial expenditure of energy.

In quantum theory, collisions that violate the principle of conservation of energy can still take place for short periods, but their effect is less if the unbalance of energy is large. The exclusion principle, therefore, substantially reduces the mutual interference of the particles with each other's motion.

It is therefore, reasonable to picture each nucleon as moving freely. Its energy will be affected by its general surroundings, but not by accidental encounters with other individual nucleons. This picture is the same as the 'shell model' used in finite nuclei, in which, as in the shell model for atoms, each particle is assumed to pursue a definite orbit in a field of force. The great success of the shell model in describing nuclei and their spectra appeared puzzling, in view of the strong short-range forces between nucleons, until the role of the exclusion principle in suppressing the interactions was appreciated.

It would now be natural, in computing the motion of each nucleon, to take the field of force as the average of the force due to all other nucleons, also taken as moving independently. This is the method of Hartree and Fock, which has been used very successfully for the electrons in atoms. A literal application to the nucleus is, however, ruled out by the short-range repulsion.

The repulsion makes the potential energy of the mutual interaction between two nucleons practically infinite at close approach. In their actual motion, nucleons will therefore keep apart and not penetrate each other. But in the hypothetical independent motion, which underlies the Hartree-Fock approximation, nucleons would occasionally be found very close together. While this would occur only rarely, the strength of the consequent interaction, when it does happen, is large enough to disturb the average and create a computation problem.

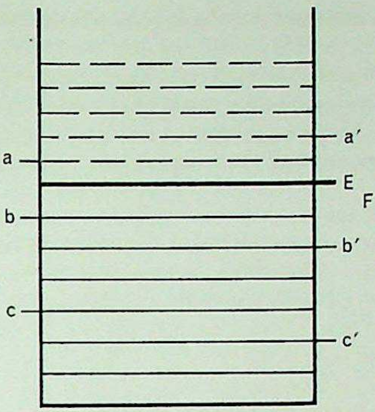

Figure 3 Nucleon energy levels (schematic).

This difficulty was resolved by the method developed by K. A. Brueckner and further elaborated by many others [5]. This rests on the fact that the range of the repulsion is very short compared with the mean distance between nucleons. If, therefore, two nucleons approach sufficiently closely for the repulsion to occur, it is unlikely that a third nucleon will also be close enough to affect the motion. The mutual disturbance of each other's motion by the repulsion of two nucleons may therefore be regarded as a rather intimate affair between the two of them.

Instead of assuming each nucleon to move in the averaged potential of the others, as in the Hartree-Fock method, it is reasonable to treat the interaction of any two nucleons as occurring in a medium representing the average effect of all others. Following this principle, it is possible—with a considerable computational effort—to work out the interaction of two nucleons and hence the energy of nuclear matter as a function of density, provided the internuclear forces are known.

These internuclear forces have been derived in fair detail from nucleon-nucleon scattering experiments, though improved accuracy may still modify the results. The values for the density and energy at normal density of nuclear matter agree well with the empirical results quoted earlier. The same calculations give the compressibility, which was quoted but which cannot easily be related to experiment.

The application of these ideas to the surface region, or to finite nuclei, presents still greater difficulties, so much so that it is not yet possible to make such calculations with confidence.

As regards the specific heat, the independence of the motion of nucleons—except for their avoiding too close approach, which appears through a modification of the forces—applies not only to the normal state but also to excited states, provided the state of excitation is not too high. This suggests that the specific heat behaves like that of liquid ^{3}He or of electrons in metals, and this in turn suggests a law of the form $E=\frac{1}{2}\gamma T^2$ A calculation of the coefficient γ from first principles is, however, not yet available.

Limitations

Our discussions of the possible transitions (figure 3) showed that such transitions were inhibited, except for two nucleons which both have energies just slightly below E_F. This makes our approximations invalid for a small fraction of the nucleons, and for an even smaller fraction of the interactions. This error is not likely to matter for the bulk properties of nuclear matter, but certain properties are sensitive to the behaviour of the most energetic nucleons. An example is the transport properties of nuclear matter, such as viscosity. It is very possible that nuclear matter might be superfluid, like the electrons in a superconducting metal. Similarly, such refinements would be important in relation to the specific heat at very low temperatures.

However, the detailed structure of the energy levels near E_F is also dependent on size, and even the heaviest nuclei are probably far too small to resemble uniform nuclear matter to the extent that this type of superfluidity would be of more than academic interest. It is, however, related to similar features occurring in the low-lying levels of finite nuclei.

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Book reviews

SCIENCE AND SOCIETY

The Department of Scientific and Industrial Research, *by Sir Harry Melville (The New Whitehall Series No. 9). Pp. 200. George Allen and Unwin Ltd, London; Oxford University Press Inc., New York. 1962. 25s. net.*

The issue of this book in 'The New Whitehall Series' prepared under the auspices of the Royal Institute of Public Administration to provide authoritative descriptions of the present work of the major departments of Central Government is most welcome for two reasons. Its issue provides a valuable account of how the D.S.I.R., founded in 1915, has met and is meeting its statutory obligation to encourage scientific and industrial research and to disseminate the results of such research. Perhaps more significantly, it is a recognition of the importance of science and technology in the life of the nation today.

This book presents a history of the origin and development of the D.S.I.R., and its organization and its activities. We are reminded that radar was born in the Radio Research Station and that Nobel Prizemen A. J. P. Martin and R. L. M. Synge were at the Wool Industries Research Association when they developed their fundamental work on partition chromatography.

Here and there in the early pages a slight air of apology is detectable. The record presented in the book, however, is one of sound achievement in the teeth of discouraging circumstances, and it should breed a boldness of outlook to deal with an even more challenging future.

D. C. Martin

Directory of British Scientists, 1963. *Pp. xxxii+1289. Ernest Benn Ltd, London. 1963. £6 6s. net.*

There has long been a need for a comprehensive directory of British scientists, and this new publication goes a fair way to meeting it. It lists some 30 000 British science graduates, giving concise biographical details, together with a list of scientific societies and their journals; of other scientific periodicals; and of research establishments.

The weakness of the work at present is its incompleteness; it probably covers only about half of those eligible for inclusion, and the absentees include some very senior scientists. For this, there seem to be two main reasons. Firstly, many of those to whom questionnaires were sent failed to return them, and the publishers very properly decided not to use information gained indirectly. Secondly, the publishers' decision to restrict entries to science graduates of British universities automatically excludes those who have entered science by way, for example, of medicine or engineering. Also excluded are those who have no university degree but have other qualifications generally looked on as fully equivalent.

Despite this, the work already contains enough information to make it widely useful, and the publishers are to be congratulated on having got so far with their first edition. If British scientists will be more forthcoming, and the publishers a little more liberal in defining a scientist, a very short time should see the evolution of a complete and very useful work of reference.

Trevor I. Williams

MATHEMATICAL PHYSICS

Methods of Mathematical Physics, *Vol. II,* **Partial Differential Equations,** *by R. Courant. Pp. xxii+830. Interscience Publishers, a Division of John Wiley & Sons, New York and London. 1962. £6 12s. net.*

This is much more than an English translation of the second part of *Methoden der mathematischen Physik*, with which mathematical physicists have been familiar for many years. The present volume contains very much more material and indeed gives a general survey of the present state of the theory of partial differential equations. We are also promised a third volume that will deal with the material in the last chapter of the German edition and in particular discuss the existence theory of elliptic differential equations. The present volume contains an admirable description of the classical theory of partial differential equations, written from a thoroughly modern standard, in which the theory of characteristics exercises a dominant role.

In dealing with differential equations of an order higher than the first, the author gives a valuable account of potential theory and of the fixed-point method of Leray and Schauder for establishing the existence of solutions of elliptic equations.

The theory of hyperbolic differential equations occupies nearly 300 pages and gives a very thorough and up to date account of the methods of wave propagation. An appendix gives a summary and critique of ideal functions and distributions.

G. Temple

ASTRONOMY

Solar Research, *by Giorgio Abetti. Pp. 173. Eyre and Spottiswoode (Publishers) Ltd, London. 1962. 18s. net.*

Solar research has passed through several changes of emphasis recently, and this book is an outstanding elementary exposition of topics that scarcely existed a few years ago. For example, instead of beginning in the traditional manner by cataloguing surface features of the Sun, the first chapter places this one star among the millions of the Milky Way, locating it in the Russell diagram that is the main evolutionary graph of astrophysics. In chapter nine this treatment of the Sun as a star, peculiar only because of our proximity to it, extends into the nuclear physics of the source of energy for solar radiation over the few thousand million years demanded by terrestial palaeontology. Between these chapters, the more conventional topics of eclipses, sunspots, and the instrumental equipment of research are also treated with the clarity always associated with this veteran Italian solar physicist. Three other recently emerging topics, which he discusses in separate chapters, are the permanent and transient radio spectrum of the Sun; the high-speed ionic emission from it that contributes to terrestrial reception of cosmic rays; and the circumterrestrial zones of ionization that control the latter.

Martin Johnson

ASTROPHYSICS

The Distribution and Motion of Interstellar Matter in Galaxies, *edited by L. Woltjer. Pp. xiii+330. W. A. Benjamin Inc, New York. 1962. $11.75.*

This most stimulating volume gives the proceedings of a conference held in April 1961 at Princeton, at which some twenty leading astrophysicists discussed the distribution and motion of interstellar gas and dust. The conference took place at the suggestion of Dr B. Strömgren, with Professor J. H. Oort as chairman. Thirty papers were read. These are published in this volume essentially as they were given, each followed by the important points of the relevant discussion. The emphasis is on interstellar gas and radio observations and, naturally, on our own galaxy, but the properties of gas in other galaxies, spiral, elliptic, and irregular, are discussed in at least three important papers. Some particularly interesting contributions deal with galactic magnetic fields and their influence on the equilibrium of interstellar clouds and on star formation. Several papers are concerned with cosmic rays, their origin and acceleration, and their effect on the motion of the interstellar gas. There are, naturally, papers on the interaction between stars and interstellar matter, involving the question of star formation and evolution, and there is a very interesting chapter in which an attempt is made to consider the evolution not only of our own galaxy, but of galaxies in general. The volume, very well edited by Dr L. Woltjer, who had acted as secretary of the conference, will be a stimulus to many astrophysicists and to all astronomers concerned with galactic research. *H. A. Brück*

DATA IN PHYSICAL SCIENCE

Handbook of Chemistry and Physics *(forty-fourth edition), edited by C. D. Hodgman. Pp. xxv+3604. Chemical Rubber Publishing Co, Cleveland, Ohio; Blackwell Scientific Publications Ltd, Oxford. 1962. £5 5s. net.*

The new edition of this invaluable reference book has, as with previous editions, been extended by the addition of new tables and revised by the correction of old. Probably the most important change is the adoption of the new atomic-weight scale, based on the ^{12}C isotope. The book gives a periodic chart, a list of recalculated fundamental constants, and a list of atomic weights, all based on the new scale.

There are more than twenty other new tables. These include tables of binary and ternary azeotropes; superconducting elements and superconducting materials other than elements; the specific conductivity of aqueous KCl solutions; equivalent conductances of other aqueous electrolytes; and data on elementary particles and their decay. Many other tables have been revised, including that of the lengths of bonds joining carbon to other elements. The book worthily follows its predecessors. *W. A. Osman*

ATOMIC PHYSICS

Atomic Physics Today, *by Otto R. Frisch. Pp. vi+254. Oliver and Boyd Ltd, Edinburgh and London. 1962. 25s. net.*

This is a collection of articles with an average length of about fifteen pages. The first four articles are connected more or less closely with civil applications of nuclear energy; the last three are concerned with parity, individuality, and causality; and the middle of the book comprises one article about atoms and seven about the techniques of nuclear physics and the many 'particles' that these techniques have made observable.

The articles have been assembled from broadcasts and separately published accounts for general readers. Their style is informal and their language so cleverly adjusted that only a few American spellings remind the British reader that the book was first published in the United States. The order of the articles has been chosen with care, even though, as the author points out, they remain independent of one another. The facts are accurate and the analogies are just, so that physicists can read the book with pleasure and indeed with profit, just as they would enjoy listening to a conversation between Professor Frisch and an interested non-scientist.

I found only one point where I should want to interrupt, to ask if Planck really thought his parcels of energy to exist as such in the radiation field. This, of course, is a question of history more than of actual physics; and since Professor Frisch's sketches are of the present scene, it is reasonable that the formidable conceptual and technical obstacles of the past should not be much emphasized.

The book contains photographs of eight of those who overcame these obstacles: Curie, Rutherford, Einstein, Fermi, Planck, Bohr, Lawrence, and Yukawa. I was particularly struck by the picture of Fermi, which captures him to the life. The photographer was O. R. Frisch. *P. B. Moon*

NUCLEAR PHYSICS

Nuclear Shell Theory, *by Amos de-Shalit and Igal Talmi. Pp. x+573. Academic Press Inc, New York and London. 1963. £5 3s. 6d. net.*

Wave mechanics gave an accurate description of atoms with comparative ease. The electrons rotate around the small massive nucleus and are held by the long-range Coulomb attraction. The spherical symmetry of the attraction gives rise to the angular momentum classification of the orbits, and Pauli's exclusion principle then imposes the electronic-shell structure, which in turn explains the Periodic Table. This very considerable advance in knowledge followed easily from the invention of wave mechanics.

There have been no such grand advances in the study of the structure of the nucleus. The nucleus is more or less homogeneous, consisting of up to several hundred protons and neutrons that have strong short-range mutual interactions. Several models of the nucleus regard the motions of the nucleons as being essentially collective—for example the liquid-drop model that Bohr and Wheeler used to elucidate fission. However, it is possible to think of each nucleon moving in an averaged field of interaction that represents the forces due to all the other nucleons. This gives the shell model of the nucleus.

This book is concerned solely with the mathematical devices used to set up the shell-model wave functions and to calculate, for example, energy levels. This is done carefully and in considerable detail. Racah coefficients, $9j$ symbols, irreducible tensors, seniority, and fractional parentage coefficients are all discussed, and numerous examples are worked out. In short, this is an excellent handbook for anyone wishing to carry out or understand shell-model calculations.

There is one criticism. Group theory is the very essence of this subject, yet it is not mentioned until near the end, and then rather briefly. The time has surely come for nuclear physicists not to be so reticent about group theory. More of it, introduced at an earlier stage, would give this book greater coherence and make it easier to read. *J. Hamilton*

NUCLEAR SCIENCE

Annual Review of Nuclear Science, *Vol. 12, 1962, edited by Emilio Segrè (Associate Editors: G. Friedlander and W. E. Meyerhof). Pp. 633. Annual Reviews Inc., Palo Alto, California. 1962. $8.50.*

One has come to expect the highest standard of contribution from the Annual Review of Nuclear Science. The twelfth volume lives fully up to this tradition, in both the excellence of the reviews and in the extreme diversity of the topics covered. These include dispersion relations in strong interactions of elementary particles (Amati and Fubini); technology of research reactors (Weinberg); nuclear astrophysics (Burbridge); atomic displacements in solids (Goland); and recoilless nuclear resonance absorption (Mössbauer). This diversity has been characteristic of the reviews all along, and it is good to have a cumulative index of volumes 8 to 12 as a supplement to the present volume. No doubt every serious nuclear library will wish to acquire this book. *A. Salam*

MAGNETISM

Fluctuation, Relaxation and Resonance in Magnetic Systems, *edited by D. ter Haar. Pp. viii+320. Oliver and Boyd Ltd, Edinburgh. 1962. 63s. net.*

This book contains the edited proceedings of the Scottish Universities Summer School in 1961. Its contents are somewhat heterogeneous—the result of a clash between two schools planned independently on the same topic for the same time, in Scotland and the Netherlands, and its resolution by dividing the field. The outcome is that the school which was to have covered the general field of fluctuations and relaxation has concentrated on magnetic systems.

There are broadly three types of contribution. First, general surveys of basic ideas, which the expert knows where to find in the literature, and which the less specialist or younger worker will welcome in the present form. Particularly to be mentioned are Callen's lectures on the fluctuation-dissipation theorem; ter Haar's on the density matrix and less well known Green's functions of statistical mechanics; and the account by Kubo of the stochastic theory of line-shape and relaxation. Then there are didactic discussions on particular topics, illustrating some principle. McCombie's article on photon fluctuations is an educative example. Finally, there are a number of recent developments in the form of pre-print accounts, for example, Callen's article on the statistical mechanics of ferromagnetism. *M. H. L. Pryce*

SEMICONDUCTORS

Thermomagnetic Effects in Semiconductors, *by I. M. Tsidil'kovskii. Pp. viii+333. Infosearch Ltd, London; Cleaver Hume Press Ltd, London. 1962. 63s. net.*

The thermomagnetic effects in semiconductors have been neglected until recently in contrast to the Hall effect and magnetoresistance. This is because of the difficulty of the theoretical analysis and because the effects are frequently small and difficult to measure. More recently, several factors have led to a marked change in the situation. Firstly, it was realised that the thermomagnetic effects represented one of the few remaining semiconductor topics awaiting detailed investigation. Secondly, it was realised, as the theory developed, that the subject could make important new contributions to the understanding of transport processes. Thirdly, it now seems clear that further progress with thermoelectric refrigeration or generation is unlikely to be spectacular; thermomagnetic refrigeration and generation are therefore now being considered.

The book defines the phenomena, reviews the literature, and presents the theory in some detail for different scattering processes for non-degenerate semiconductors. There is a short treatment of degeneracy, and a useful account of the contribution of phonon-drag. The later part of the book describes the experimental results so far available on germanium, tellurium, and on a variety of compound semiconductors, and interprets the results in the light of the theory presented earlier.

The book appears to be well written and translated, although many readers would, I believe, welcome more emphasis on the physical significance of the theory. There is, however, room for improvement in presentation. A rather faint, small type is used for the equations, the tables, and the legends for some of the diagrams, and in addition complicated suffixes are widely used. The book however can be welcomed as an important contribution to a subject in which interest is very lively at the present time.

D. A. Wright

LUMINESCENCE

Luminescence in Crystals, *by D. Curie (translated by G. F. J. Garlick). Pp. xi+332. Methuen & Co Ltd, London; John Wiley & Sons, New York. 1963. 50s. net.*

The presentation here is taut and economical. If these are Gallic virtues, then they have survived translation, and the outcome, if not easy to read, is more rewarding than the usual windy circumlocution. The first chapter is the best part of the book, bringing fundamentals into rightful prominence. The elegance of the subject is now overlaid by factual complexity, and the practical applications will hardly fire an imagination that has known the transistor. To justify itself, luminescence must be brought into the main stream of contemporary physics. This book disappoints precisely because it fails to achieve this.

The laser unfortunately appeared too late to stimulate a broader view. Even so, one could have hoped for a wider treatment of radiative recombination in semiconductors (gallium phosphide and arsenide are not mentioned). Most of twenty pages are devoted to a configurational co-ordinate model for thallium-activated potassium chloride, but important criticisms of the model must be gleaned from a reference. There is no real attempt to link luminescence with crystal field theory, but considerable space is devoted to topics whose rightful place is the kitchen, not the laboratory.

G. F. Alfrey

CHEMICAL CALCULATIONS

The Mole Concept in Chemistry, *by William F. Kieffer. Pp. ix+118. Chapman and Hall Ltd, London; Reinhold Publishing Corporation, New York. 1962. 16s. net.*

This book gives a practical interpretation of the mole concept in chemical terms. The author writes for the American college student to whom he is attempting to sell his ideas. English readers should be put off neither by this limitation, nor by colourful references to such people as 'sophisticated upperclassmen' and 'quiz section examiners' who have no place in the subdued and conventional scene of English academic life.

In developing the theme of the mole as a unifying concept in physical chemistry, the author makes full use of 'quantity calculus'. This method forces the student to think carefully about the units he is using, but it can be confusing initially to those who have had no experience of it. Most of the calculations in this book could be done equally well by the unitary method. The use of quantity calculus should not be allowed to distract the reader from the main theme.

The case for the mole as a central theme in chemistry, displacing the traditional equivalent weight, atomic weight, and gram molecule approach, is persuasively argued. In this way, the teaching and understanding of many phenomena can be simplified considerably. The properties of solutions, relative vapour pressures, and dissociation are good examples. On the other hand, some confusion could arise from the use of the terms molar, molal, and normal.

The book contains a great deal that is of interest to teachers of chemistry at all levels. They should read it and read it carefully.

M. J. W. Rogers

THERMOCHEMISTRY

Reaction Heats and Bond Strengths, *by C. T. Mortimer. Pp. xii+230. Pergamon Press, Oxford. 1962. 35s. net.*

The energetic aspect of molecular structure has been somewhat neglected in the scientific literature, and we are therefore especially grateful for this useful and informative little volume. Considerable original thought, as well as much care, has gone into its creation. The first chapter, 'The thermochemical approach', is really introductory, although it also includes a brief description of some specialized calorimeters of recent design. Then follow chapters on strain energies, stabilization energies, resonance energies, polymerization energies, molecular addition compounds, bond dissociation energies, metal-carbon and metal-halogen bonds, ionization energies in solution, and the effect of *d* orbitals on bond strength. The emphasis is on experimental results and on the deductions that can be made from them. There are some particularly welcome features, such as a recognition of the importance of reorganization energies of molecular fragments, and also a demonstration that 'resonance energies' cannot be uniquely derived from thermochemical measurements, because incorporated in the latter are not only delocalization energies, but other effects such as bond compression.

The clear and unpretentious style of the author adds to the enjoyment of reading. The book has 345 references and is well indexed. *L. H. Long*

INORGANIC CHEMISTRY

Theoretical Inorganic Chemistry, *by M. Clyde Day and Joel Selbin. Pp. xiv+413. Reinhold Publishing Corporation, New York; Chapman and Hall Ltd, London. 1962. 96s. net.*

The authors of this book obviously have the right ideas about the teaching of inorganic chemistry. They believe in trying to relate awkward facts to physico-chemical principles. The first third of the book is devoted to an elementary exposition of quantum chemistry. There follow chapters on inorganic stereochemistry, electromotive force (*sic*), acids and bases, coordination chemistry, and non-aqueous solvents. The last chapter of the book is a long one entitled 'Theory of the nucleus',

Perhaps it will not seem ungracious to criticize the book on two main counts. First, is it not a little odd for a book on theoretical inorganic chemistry to include a long chapter on nuclear physics, but to omit any reference whatever to the boron hydrides, which played a prominent role in the theory of chemical bonding? Secondly, there is a distressing lack of coherence between the theory expounded in the early part of the book and the more experimental chapters which follow. The student might well be baffled by the introduction of so much mathematical material when very little of it is actually used for interpreting the diverse facts of inorganic chemistry. But when all is said and done, the authors are to be commended for recognizing the importance of theory in the interpretation of chemical facts, even if they are not altogether successful in integrating quantum chemistry with the phenomena that one observes in the laboratory.

H. C. Longuet-Higgins

FLUORINE CHEMISTRY

Advances in Fluorine Chemistry, *Vol. III, edited by M. Stacey, J. C. Tatlow, and A. G. Sharpe. Pp. 281. Butterworths, London. 1963. 50s. net.*

The third of this series of monographs maintains the high standard of the earlier volumes. Six major topics are dealt with and, as before, the authors are authorities in their respective fields. Two of the chapters, on the effects of adjacent perfluoroalkyl groups on carbonyl reactivity and on the mechanisms of fluorine displacement, reflect the growing interest in the influence of highly negative fluorine-containing groups on reactivity. Dr Clarke's article on perfluoroalkyl derivatives of the elements contains a detailed review of this rapidly expanding new field, and it has been brought almost up to date by an addendum that summarizes work published since 1961. One of the most interesting contributions is Dr Colburn's account of the nitrogen fluorides and their inorganic derivatives. Carbon tetrafluoride and a few of its simpler homologues represented at one time the full extent of our knowledge of fluorocarbons, but the subject has now grown tremendously. In much the same way, though on a smaller scale, the chemistry of nitrogen trifluoride and related compounds is being extended rapidly, and some of the more recent developments are described here.

The last two sections are perhaps the most generally interesting. The first deals with the preparation of organic fluorine compounds, both aliphatic and aromatic, by halogen exchange, and the second with the organic fluorochemicals industry. They serve to illustrate both the extent to which these fields have developed in recent years and the growing range of technical applications of a variety of fluorochemicals.

H. J. Emeléus

INORGANIC POLYMERS

Inorganic Polymers, *edited by F. G. A. Stone and W. A. G. Graham. Pp. xi+631. Academic Press, New York and London. 1962. £6 19s. 6d. net.*

Unfortunately, this is not the book that the reviewer had hoped for. It is a useful multi-author work, with some first-class stimulating reviews of areas of current interest; but it sadly lacks an overall critical approach, and it fails to inspire or to point out what lessons have been learned and whither future endeavour should or might be directed: the threads have not been pulled together. The editors devote only eight pages of introduction to general principles and comments before plunging into a series of unconnected articles on polymer properties (Tobolsky); polymers of phosphorus (van Wazer), sulphur (Schmidt), and boron (McCloskey): silicone polymers (Barry and Beck), and those of silicon, germanium, tin, and lead (Ingham and Gilman): and metal-oxygen polymers (Bradley), co-ordination polymers (Block), and electron-deficient polymers (Leffler). As with most books of this type, the standard and approach vary widely from chapter to chapter. The accent is often on preparative aspects, and there is no separate account of the use of physical methods, or of problems of characterization and analysis; the fact that some of the polymers might and do find use is usually ignored. The great amount of current interest and effort in the field of inorganic polymers justifies a series of monographs on the subject; the present book makes a brave, well-produced, though expensive, beginning.

R. N. Haszeldine

CHROMATOGRAPHY

Thin Film Chromatography, *by E. Vernon Truter. Pp. xi+205. Cleaver-Hume Press Ltd, London, 1963. 37s. 6d. net.*

Laminar chromatography is the most recent addition to the range of chromatographic techniques, and it already finds widespread use in many laboratories. The author distinguishes between thin-layer chromatography, wherein the solid particles are loose, and thin-film chromatography, in which a coherent layer is formed. The former name is widely employed to cover both situations, although relatively little work is done with loose layers.

The approach of this book is strictly empirical and so, while it is a storehouse of practical information, the reader will have to look elsewhere for a proper understanding of the processes occurring. However, within these self-imposed limitations, the author has produced an admirable account and the book is very likely to find wide use as a laboratory manual.

The three major sections are fundamentals, special techniques, and applications. Fundamentals, in this context, are essentially basic operating techniques, and these are described clearly, and at some length. This section describes the preparation and choice of films, sample spotting and development, and, in qualitative terms, the effect of conditions on R_f.

The special techniques section describes multiple-stage and two-dimensional development, the effect of pH, partition as opposed to adsorption films, and quantitative methods. The last section describes the use of ancillary techniques and gives an account of the separation of numerous complex mixtures.

After reading this book, anyone should be able to undertake this form of chromatography with success, and on this account it is recommended. The format is pleasant and free of error.

J. H. Purnell

GAS CHROMATOGRAPHY

Gas Chromatography. Principles, Techniques, and Applications, *by A. B. Littlewood. Pp. xi+514. Academic Press, New York and London. 1962. £5 7s. 6d. net.*

The arrangement of this book is precisely what one would expect of the author—it is a careful, well arranged physico-chemical approach that covers in detail the major fundamental aspects of the subject. The first six chapters range from an introduction to gas chromatography to a basic treatment of column performance. Four chapters deal with detectors and ancillary apparatus, and the final chapter is a rather potted coverage of applications. There are a few mistakes in this last chapter, but on the whole most of the relevant references are quoted. Three indexes are provided, to authors, subjects and chemicals. The book is well written and adequately illustrated and can be recommended to anyone seriously taking up the technique. It is one of the best books on this subject.

A. T. James

CHEMICAL LINGUISTICS

German–English Chemical Terminology, An Introduction to Chemistry in English and German, *by H. Fromherz and A. King (fourth revised and enlarged edition). Pp. xxi+588. Verlag Chemie GmbH, Weinheim/Bergstr., Germany. 1963. DM 48.*

The present edition of this book has been largely rewritten, and some sections on contemporary ideas on atomic and nuclear structure and the nature of chemical forces have been added. The two texts are printed side by side on opposite pages, and expressions appearing for the first time are printed in italics in both texts. The index of 10 000 terms in English and German contains all the expressions printed in italics in the text with the page number and a letter indicating its position on the page. This will be valuable if the book is used instead of a dictionary. There is an appendix on mathematical expressions, one giving English abbreviations and one giving German with their equivalents in the other language, and a list of English expressions with phonetic pronunciation.

The book is described as a more or less comprehensive introduction to chemistry. It begins on the level of a school textbook, but the later sections are not really informative and serve only to introduce modern scientific terms in both languages. The book will be helpful to English- or German-speaking scientists who have to use literature in the other language, and to translators or interpreters if they have some basic knowledge of chemistry.

G. T. M. Schlesinger

Chemie im Dienst der Archäologie, Bautechnik, Denkmalpflege, *by J. Arvid Hedvall. Pp. x+226. Akademiförlaget-Gumperts Göteborg. 1962. 95 Sw. Kr.*

This is a unique book for all aspiring universal men. It reaches far beyond its title in a heroic attempt to promote, in its own fashion, co-operation between the humanities and the sciences. This attempt, which the author modestly calls 'tentative', is in fact as penetrating and comprehensive as it could be within the framework of the book. Its two-pronged attack aims to inoculate the humanities with a basic material understanding of material culture, and at the same time to excite the basic resonance frequencies of interest in even the most highly specialized men of science. The implication is clear. The heritage and responsibility alike rest squarely on the shoulders of every one of us. Yet most of us still need cajoling into a receptive state of mind.

It is this that the author, a world-famous authority on the solid state, sets out to do in an ingenious and original manner on an incredibly broad front. We are given, in effect, a guide to the physical chemistry of antiquities, past and future. The book was commissioned by the Academy of Sciences and Literature at Mainz, who deserve our praise and gratitude for a venture so far-seeing and universally valuable. The author travelled all over Europe and assembled other first-hand information by correspondence with authorities directly concerned with these problems all over the world.

There are three main parts: condition of important monuments; structure of materials; and deterioration, restoration, and conservation—but they are permeated throughout by a physico-chemical miniature of the world's treasures. What emerges most clearly, perhaps, is the overriding importance of interfaces, and of the mutual effects of dissimilar materials. A highly stimulating and somewhat disturbing book.

L. Biek

GEOPHYSICS

Physique solaire et géophysique, *by A. Dauvillier. Pp. 362. Masson et Cie, Paris. 1962. 72 F.*

The reasons for present interest in physics, and particularly in solar physics, are obvious, and make the publication of this book particularly valuable now. The information given in it about the constitution of the Sun is, intentionally, only that required to understand the succeeding chapters, which are based on the connection between solar and terrestrial phenomena. These chapters open with a discussion of solar magnetism, for which none of the explanations given seem plausible, followed by a chapter devoted to the author's own theory. The study of the corona and its variations, and of zodiacal light, lead to sections on terrestrial phenomena that originate with the Sun—the aurora, geomagnetism, cosmic rays, and the Pleistocene glaciation. The book is a valuable synthesis of a large amount of research. It is well illustrated and has a useful bibliography.

J. Roger

Principles of Applied Geophysics, *by D. S. Parasnis. Pp. ix+176. Methuen & Co Ltd, London John Wiley & Sons Inc., New York. 1962. 21s. net.*

Unlike the standard textbooks on applied geophysics, this recent addition to 'Methuen's Monographs on Physical Subjects' does not demand an extensive knowledge of mathematical physics on the part of the reader. The geologist or engineer who wishes to know how he might profitably make use of the services of a geophysicist may obtain such knowledge with a minimum of effort from this brief but comprehensive outline of the principles and methods of geophysical prospecting. In addition to the well established divisions of applied geophysics, this book covers several of the latest innovations which, to date, have been described only in the journals. Because of the size and scope of the book, it is impossible for the author to treat any particular subject in detail, but an adequate bibliography is provided for the reader who requires further information.

Robert B. Roden

METEOROLOGY

Exploring the Atmosphere, *by G. M. B. Dobson. Pp. xi+188. Clarendon Press; Oxford University Press, London. 1963. 21s. net.*

There are very few good, even sound, popular books on meteorological subjects, so this collection of essays by Professor Dobson on physical phenomena in the atmosphere is especially welcome.

In the short space allotted in the book to each topic it is not possible to do more than describe the main facts of observation and to outline the techniques by which these have been established. This is done clearly and dispassionately, without mathematics, using language that should be comprehensible to anyone studying physics at Sixth-Form level. As one would expect, the most successful chapter is that in which Professor Dobson describes the formation, distribution, and transport of ozone in the atmosphere, a field in which he has been the leading authority for over forty years. Not that there is a single clue to the latter fact in the whole book, for the author has been careful to exclude names and personalities. This gives the text a curious, rather dry flavour, perhaps a little disturbing for the novice who does not trust his nose and palate, but only the label on the bottle. It is also a pity that Professor Dobson has not included a few well-chosen photographs, which could have given point to his text and added greatly to its appeal. Even so, this book is good value as it is, and should find a place in school and public libraries.

B. J. Mason

CELL RESEARCH

The Interpretation of Ultrastructure, *edited by R. J. C. Harris* (Symposia of the International Society for Cell Biology, *Vol. 1*). *Pp. x+438. Academic Press, New York and London. 1962. £5 net.*

In earlier years, the papers presented at the annual symposia of the International Society for Cell Biology have been published as supplements to 'Experimental Cell Research'. Commencing with the 1961 symposium, they are being published in the form of separate books, so as to obtain a wider circulation. This book is the first of this new series. The aim of the 1961 symposium was to assess as critically as possible the meaning of the images seen in electron micrographs. The basic questions are: which images can be regarded as reasonably true, and what biological significance can be attached to them? These questions have always troubled cytologists, and quiescent periods of acceptance have generally alternated with more violent ones of rejection. Today, however, the problems are so complicated that rigorous reappraisement is slow and often uncertain. Yet it is essential, and leads to even more exciting, better founded theories; it is all this that makes the book, no less than the symposium that it represents, so valuable. The contributors are all well-known international authorities. There are 22 chapters, mostly with short discussions, whose subject matter ranges from a technical assessment of various methods such as chemical fixation, freeze drying, enzyme localization, and negative staining, to the biological re-evaluation of what they demonstrate There are many beautiful illustrations, mostly electron micrographs. The book is indeed a worthy first volume.

Dennis Lacy

SENSORY RECEPTORS

Biological Receptor Mechanisms (Symposia of the Society for Experimental Biology, *No. XVI*). *Pp. vii+372. Published for the Company of Biologists on behalf of the Society for Experimental Biology at the University Press, Cambridge. 1962. 50s. net.*

The range of the capabilities of the eye, ear, and certain proprioceptors was discussed at a conference in 1950. This 16th symposium of the Society of Experimental Biology, twelve years later, provided a timely occasion for workers in several disciplines to present the subsequent results of their studies of the organs of special sensation in various animals.

Almost half the volume is devoted to accounts of the eye and of the way that living things respond to light. There are also individual contributions on, for example, olfaction; chemical, electrical, and temperature reception; gravity perception in plants; and mechanoreception in mammals. Finally, an account is given of the significance of the encoded nerve-impulse signals sent to the brain by certain peripheral receptors.

It is a pity that so few optical and electron micrographs of receptors illustrate this stimulating volume, since the interpretation of new physiological data and the satisfactory elaboration of fresh theories of function depend on precise knowledge of structure.

The quickening pace at which fresh information in these and various related fields is accumulating leads one to hope that the interval before the next symposium on sensation will be much shorter than previously.

T. A. Quilliam

OXIDIZING ENZYMES

Oxygenases, *edited by Osamu Hayaishi. Pp. xii+588. Academic Press, New York and London. 1962. £6 5s. net.*

The editor of this volume is one of the pioneer investigators of the group of oxidizing enzymes that catalyse reactions in which molecular oxygen is activated and incorporated into the product. The book is a collection of review articles. It begins with an historical survey by the editor that outlines in clear terms the position of this class of reactions in the much wider group of enzymes responsible for biological oxidation. The book continues with more detailed and specialized articles by different workers, covering methodology and specific examples and groups of oxygenases. These provide a valuable and lucid guide to the state of knowledge in this comparatively new field and should do much to stimulate further work. With the expressed purpose of leading to an overall clarification of oxygen metabolism in general, one third of the volume is devoted to peroxidase, cytochrome oxidase, and respiratory pigments concerned with oxygen transport. These articles, like the ones concerned with oxygenases proper, are erudite and informative. However, all the chapters except the introduction are highly specialized; one might have hoped in a book with such a purpose for more attempts at integration and generalization.

Vincent Massey

ALGAE

Physiology and Biochemistry of Algae, ***edited by Ralph A. Lewin. Pp. xxvii+929. Academic Press, New York and London. 1962. £11 9s. net.***

Not since 1923 has there been an attempt to review the physiology and biochemistry of the algae, although these are topics in which many advances, fundamental to plant science, have been made. This book consists of 55 chapters, each written by an expert, and is split into four sections: nutrition and metabolism; composition of cells and metabolic products; physiology of whole cells and plants; and physiological aspects of ecology; together with very brief appendices on classification, uptake of radioactive waste, and antibiotics. The chapters vary in size and few exceed twenty pages, yet the overall impression is that of a book rather than a review, although there is little explanatory matter for the non-specialist. The editor admits in the preface that authors were limited to a certain number of words, and some of the chapters obviously suffer from this, while on a few topics there is as yet so little known that it might have been better to give the space to others. Most of the chapters were complete by mid-1960, with some additions of data from the succeeding year, but nevertheless this is a welcome, well produced compilation of otherwise scattered data, and it will undoubtedly stimulate research on some of the lesser known aspects.

F. E. Round

PLANT TAXONOMY

Plant Taxonomy, Methods and Principles, ***by Lyman Benson. Pp. ix+494. The Ronald Press Company, New York. 1962. $11.50.***

There are some books devoted to orthodox taxonomy, and some devoted to biosystematics. This is the first I have seen that attempts to deal comprehensively with both. It assumes an elementary knowledge of plant classification, and can be regarded mainly as a guide to advanced students and research workers. The author shows that data from field observations, microscopic morphology, palaeobotany, physiology, chemistry, ecology, and cytogenetics, as well as herbarium studies, can and should be utilized as far as possible in a taxonomic study. He goes on to deal with the principles of classification, and with the tricky problems of nomenclature, keys, and the type method. He discusses finally how a monographic study should be tackled and the results presented. There are extensive and informative bibliographies, and a comprehensive index. The illustrations are numerous and well chosen.

There is a real need for a book of this type, and although the attempt to cover the whole field has inevitably resulted in a superficial and sometimes unsatisfactory treatment of some aspects, this volume is welcome. Most of the examples chosen are Californian, but the same principles apply to plants elsewhere, and this is the flora that the author knows best and can describe most expertly. I can recommend this book.

S. R. J. Woodell

PLANT PHYSIOLOGY

An Introduction to Plant Physiology ***(sixth edition), by W. O. James. Pp. viii+329. Clarendon Press; Oxford University Press, London. 1963. 17s. 6d. net.***

Some 24 extra pages and much rewriting have added a great deal to the previous edition of 1955. The biggest changes affect accounts of the protoplast (fine structure); respiration (new section on pentose phosphate and glyoxylic acid cycles); and photosynthesis (carbon path). Lesser changes are in the chapters on nitrogenous compounds, growth, irritability, water, and translocation. There is a very brief reference to DNA and RNA. The sections on stomatal mechanism, mineral nutrition, and photoperiodism remain unchanged. Four additional experiments are described, mostly involving plant hormones, but otherwise the experimental side of the book is essentially the same. The bibliography does not mention the valuable biological reprints from 'Scientific American', which cover most of the topics in this sixth edition. The word photosynthesis has been dropped from the index, which lists ribulose diphosphate as well as ribulose 1,5,diphosphate. For the first time the publishers do not give the history of the book. I still have my copy of the first edition, which appeared in 1931, when it was an outstanding contribution with no serious rivals.

F. B. Hora

PLANKTON

Nature Adrift, the Story of Marine Plankton, ***by James Fraser. Pp. v+178. G. T. Foulis & Co. Ltd, London. 1962. 45s. net.***

Formerly studied by only a handful of naturalists, plankton has become the preoccupation of many workers studying the fundamentals of the sea fisheries of the world. Apart from this, the animals and plants are subjects of great academic interest and of extreme beauty. However, they die very rapidly and are difficult for the layman to identify. This, together with the lack of semi-popular literature, probably largely accounts for the lack of amateur interest in them. Dr Fraser goes some way to overcome these drawbacks. He gives an up-to date outline of the natural history of many of the common species, and gives a good account of aspects of such theories as Tucker's theory of eel migrations. He writes with particular authority on indicator species. The illustrations show most of the common planktonic forms, and for these alone the book will certainly be used as a handy reference work by amateurs and by serious students of marine biology. A bibliography of key works for identification and further reading would be valuable and should certainly be included in future editions. The volume is to be recommended to all those with an interest in the sea and the life therein.

Peter S. B. Digby

LEARNING IN ANIMALS

Learning and Instinct in Animals, ***by W. H. Thorpe (revised and enlarged edition). Pp. x+558. Methuen & Co Ltd, London. 1963. 63s. net.***

This excellent book has been brought up to date without changing its fundamental plan or themes. It is significant that some of the passages that are most changed are those dealing with exploratory behaviour and 'drive'. Much physiological information on these matters has accumulated in recent years. The section on mechanisms of learning has also been considerably expanded, to include work on reinforcement centres and self-stimulation.

The largest increases are, however, in the third part of the book, in which the learning abilities displayed by the main animal groups are systematically considered. This, like the whole book, is especially valuable because it brings together data for mammals, known mostly to psychologists, and those for lower vertebrates and invertebrates, usually dealt with by zoologists. Dr Thorpe describes this great range of experiments with such admirable care and economy that his work can be used both as a textbook and for reference. It is interesting that he has not felt it necessary to make any change in the short final 'Conclusion'.

J. Z. Young

FRESHWATER FISH

Freshwater Fishes of the World, ***by Günther Sterba (translated and revised by D. W. Tucker). Pp. 878. Vista Books, London. 1963. 70s. net.***

Dr Tucker has rendered a great service by translating and revising this work. After a clear and easily understood introduction outlining the criteria required for identification, 1300 species of lampreys and teleost fishes are described. Nearly all of them are illustrated, using more than five hundred excellent colour and black-and-white photographs and many carefully delineated drawings of equal quality. These, however, are not in sequence with the text and are numbered only in the legends. While this arrangement is pleasing in appearance, it does not facilitate reference.

It is a book designed primarily for the aquarist, but is of wider scope. Descriptions are concise, adequate for identification, and enlivened by notes on habit and behaviour that, together with the illustrations, stimulate interest in ethology and evolution.

Treatment of families on a regional basis and the inclusion of maps showing distribution are of value to the zoo-geographer, but emphasis on fishes for the aquarium has produced an imbalance in the treatment of certain families. For example, species that are of economic importance in Cyprinidae and Coregonidae are disregarded. This defect is largely offset by the well chosen bibliography. *H. D. Slack*

INSECT PATHOLOGY

Insect Pathology, An Advanced Treatise,
Vol. I, edited by Edward A. Steinhaus. Pp. xvii+
661. Academic Press, New York and London.
1963. £6 16s. net.

Disease is so fundamental a feature of life that no biologist can afford to ignore it. Fortunately our ignorance of its nature and effects among invertebrate animals does not extend to the insects, and the present volume (the first of two) indicates how large a body of literature already exists on this subject.

Pathology is here interpreted widely to include physical and chemical injuries, tumours, and nutritional and genetic disorders, as well as the more familiar infectious diseases. Of the latter, only the virus diseases are treated in the present volume, but space has been found for certain general topics, including immunity; factors predisposing insects to disease; the microorganisms of healthy insects; and the role of pathogens of plants and animals as agents of disease in their insect vectors.

It is inevitable that in a comparatively young branch of science, some of the data are heterogeneous and inconclusive, but in certain fields (notably in the chapters devoted to virus diseases), there is much of fundamental interest.

Each chapter has been written by a leading worker in its particular field and is therefore authoritative. The bibliographies are extensive and the book well produced and remarkably free from typographical errors. It should prove a valuable work of reference to general entomologists and ecologists, as well as to the specialist in insect pathology.

N. H. E. Gibson

HISTORY OF SCIENCE

Great Chemists, *edited by Eduard Farber.*
Pp. xxvi+1642. Interscience Publishers, a
Division of John Wiley & Sons, New York and
London. 1962. £11 2s. net.

Apart from some introductory essays on Babylonian chemists and on Arabic (more properly described as Muslim) chemists, and four 'Interludes' by the editor, this large volume contains 108 biographies of famous chemists of the last four centuries, from Paracelsus to W. H. Carothers. Living chemists have been excluded. Two biographies deal with two great names together, Libavius and Beguin, and Dumas and Wurtz, and one deals with five American chemists 'at the turn of the century', Babcock, Wiley, Remsen, T. W. Richards, and E. F. Smith. Portraits are reproduced with a few other illustrations and some text figures; and there is an introduction, an epilogue, and a good index. The choice of names to be included in a work of this sort must always be difficult, and some readers may find it disappointing that Laurent, Gerhardt, Williamson, and Travers receive only incidental mention. Others may rightly be astonished at Black's being described (p. ix) as an Englishman. The biographies have not all been specially written for this book; many are reproduced from contemporary obituaries and addresses; ranging over two and a half centuries; and thus some modern compilers rub shoulders with such classical masters of words as Fontenell and Brougham. A useful reference work.

Douglas McKie

The Principal Works of Simon Stevin, *Vol. III.*
Astronomy, *edited by A. Pannekoek;*
Navigation, *edited by Ernst Crone. Pp. v+632.*
N. V. Swets & Zeitlinger, Amsterdam. 1962.
£9 net.

The present volume contains five of Stevin's printed works, complete or in part: *De Hemelloop* ('The Heavenly Motions'), *Van de Spiegheling der Ebbenvloet* ('On the Theory of the Tides'), *De Havenvinding* ('The Havenfinding Art'), *De Zeijlstreken* ('The Sailings'); and *De Wijsentijt* ('The Age of the Sages'). As in preceding volumes of this splendid and convenient edition, the original text—in this case in Dutch throughout—is printed on left-hand pages with an English translation opposite. These English versions by Miss C. Dikshoorn are invariably idiomatic and clear; a few mistakes (like 'proper motion', p. 107) are not at all distracting. The various treatises are well introduced and the omissions from them plainly indicated. The late Professor Pannekoek's remarks are certainly brief, but Stevin's writings on astronomy and the tides, interesting as they are, are not of the first importance. Dr Crone, however, has supplied a longer monograph on Stevin's navigational writings in their historical setting. This book is a valuable addition to the original material for the study of early seventeenth-century science and technology, worthy of one of the great men of Dutch history. *A. Rupert Hall*

William Herschel, *by Angus Armitage* **(British**
Men of Science. *General Editor. Sir Gavin de*
Beer.) Pp. xii+158. Thomas Nelson & Sons Ltd
Edinburgh. 1962. 15s. net.

Writing with the same lucid style that distinguished his earlier book, *Copernicus*, Angus Armitage has produced a sound and interesting book on one of the greatest of British astronomers, Herschel. After a brief sketch of the background in astronomy, and a biography, the book describes in detail the various aspects of Herschel's work. There is an epilogue, mentioning later work in the same tradition.

Although his most famous achievement was the discovery of the planet Uranus, Herschel's basic problems—the detection of the Earth's orbital motion, the Sun's absolute motion, and the distribution in space of the 'fixed stars'—concerned the structure of the Universe. A certain amount of technical explanation is necessary to make these problems comprehensible; this is accomplished with elegance by the author.

The only weakness in the book is that its style gives an air of calm achievement to what was a truly heroic endeavour. Herschel's work was a continuous struggle to improve his instruments and his theories to the very limits of their power. His failures are no less significant than his successes, and closer analysis of these might have produced a more exciting book. *J. R. Ravetz*

HISTORY OF MEDICINE

Medicine and the Navy 1200–1900, *Vol. IV,*
1815–1900, *by C. Lloyd and J. L. S. Coulter.*
Pp. xi+300. E. & S. Livingstone Ltd, Edinburgh
and London. 1963. 50s. net.

This fourth volume of 'Medicine and the Navy' is by the same authors as Volume III, which covers the period 1714–1815 and was reviewed in *Endeavour* in October 1962. The present work fully maintains the high standard of scholarship of the earlier volumes. Its arrangement resembles that of Volume III rather than Volumes I and II, being not strictly chronological, but as the authors state, 'divided into chapters dealing with individual themes'. There is a ten-page bibliography, of both manuscript and printed sources, and a good index. The book, like earlier volumes, is a scholarly work written in an attractive manner. It gives many details such as the uniform of the sick-berth staff, conditions of life on the Arctic voyages and on the Australian convict ships and, in a lighter vein, the origin of the term 'Fanny Adams'.

Although this volume completes the medical history of the Navy for the period 1200–1900 as originally planned by the late Surgeon-Commander Keevil, is there not now a case for a further volume on similar lines covering the period since 1900?

G. E. Trease

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Some books received

(*Note.* Mention of a book on this page does not preclude subsequent review.)

GENERAL SCIENCE

An Introduction to the Philosophy of Science, *by Arthur Pap. Pp. xiii+444. Eyre and Spottiswoode Ltd, London. 1963. 70s. net.*

MATHEMATICS

Elements of Tensor Calculus, *by A. Lichnerowicz (translated from the French by J. W. Leech and D. J. Newman). Pp. viii+164. Methuen & Co. Ltd, London. 1963. 21s. net.*

Group Theory. The Application to Quantum Mechanics, *by Paul H. E. Meijer and Edmond Bauer. Pp. xi+288. North-Holland Publishing Co., Amsterdam. 1962. 60s. net.*

Representations of Groups, *by Herman Boerner. Pp. xii+325. North-Holland Publishing Co., Amsterdam. 1963. 80s. net.*

ASTRONOMY

Astrophysique *by E. Schatzman Pp. 149. Masson et Cie, Paris. 1963. Paperback 24 F, Cloth covered 29 F.*

The Planet Mercury, *by Werner Sandner. Pp. 94. Faber and Faber, London. 1963. 21s. net.*

The System of Minor Planets, *by Günter D. Roth (translated from the German by Alex Holm). Pp. 128. Faber and Faber, London. 1962. 25s. net.*

PHYSICS

Adsorption and Collective Paramagnetism, *by Pierce W. Selwood. Pp.ix+189. Academic Press Inc., New York and London. 1962. 60s. net.*

The Concept of the Positron, *by Norwood Russell Hanson. Pp. ix+235. Cambridge University Press, London. 1963. 32s. 6d. net.*

Formal Structure of Electromagnetics, *by E. J. Post. Pp. xiv+204. North-Holland Publishing Co., Amsterdam. 1962. 40s. net.*

An Introduction to Vacuum Technique, *by A. H. Turnbull, R. S. Barton, and J. C. Rivière. Pp. x+190. George Newnes Ltd, London. 1963. 50s. net.*

Physics for Engineers, *by G. F. Lewin. Pp. xii+310. Butterworth & Co. (Publishers) Ltd, London. 1963. 50s. net.*

X-ray Optics, *by A. J. C. Wilson. Pp. vii+147. Methuen & Co. Ltd, London. 1962. 21s. net.*

CHEMISTRY

L'analyse des silicates, *by I. A. Voinovitch, J. Debras-Guédon, and J. Louvrier. Pp. 510. Hermann, Paris. 1962. 48 F.*

The Application of Organic Bases in Analytical Chemistry, *by E. A. Ostroumov (translated from the Russian by D. A. Paterson). Pp. xxv+159. Pergamon Press Ltd, Oxford. 1962. 50s. net.*

Cahiers de synthèse organique, *by Jean Mathieu, André Allais, and Jacques Valls. Vol. X. Pp. 560. Masson et Cie, Paris. 1962. 180 F.*

Elements of General and Biological Chemistry, *by John R. Holum. Pp. ix+470. John Wiley & Sons, London and New York. 1962. 45s. net.*

Elements of Physical Chemistry, *by Samuel Glasstone and David Lewis. Pp. v+758. Macmillan & Co Ltd, London. 1963. 25s. net.*

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